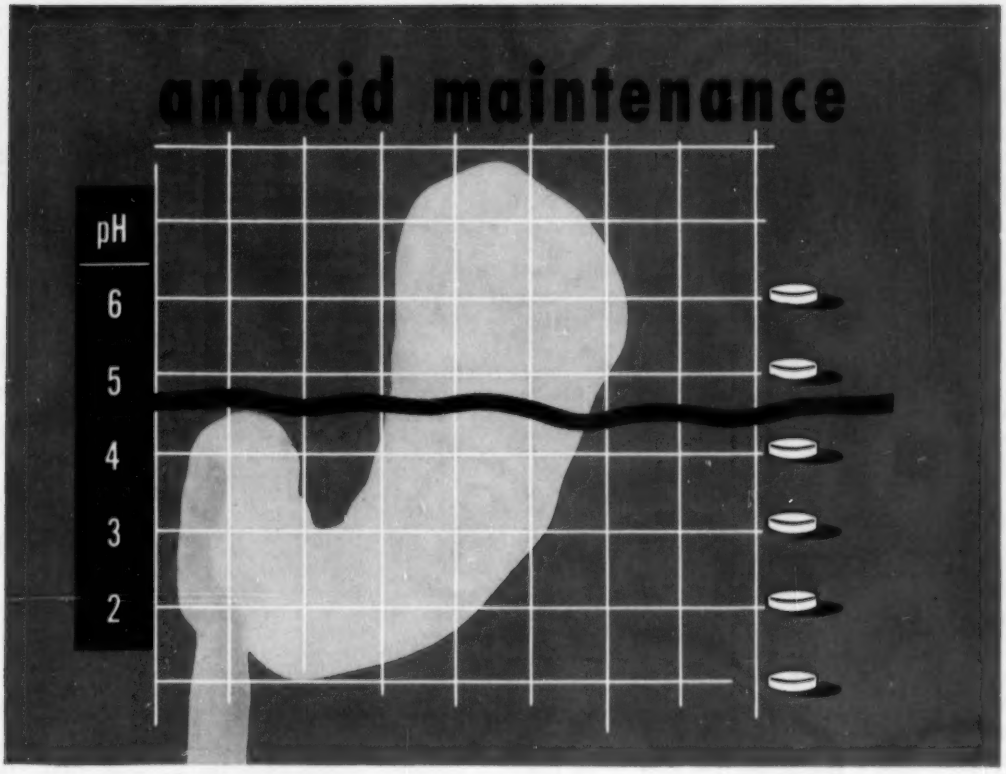
The American Journal of DIGESTIVE DISEASES

An Independent Publication

DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION

ORIGINAL CONTRIBUTIONS

Volume 22 October, 1955 Number 10



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Business and Editorial Office:
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SUITE 302-310
FORT WAYNE, INDIANA

Printing Office:
117 E. MAIN ST.
BERNE, INDIANA

Associate Editor: FRANZ J. LUST,
17 E. 89TH ST., NEW YORK, N. Y.

Advertising Office:
VINING & MEYERS
35 EAST WACKER DRIVE
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ANNUAL SUBSCRIPTION RATE $6.00; TWO YEARS, $10.00
SINGLE COPIES: CURRENT YEAR 80c. BACK YEARS $1.00.
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Published Monthly at 117 East Main St., Berne, Ind.

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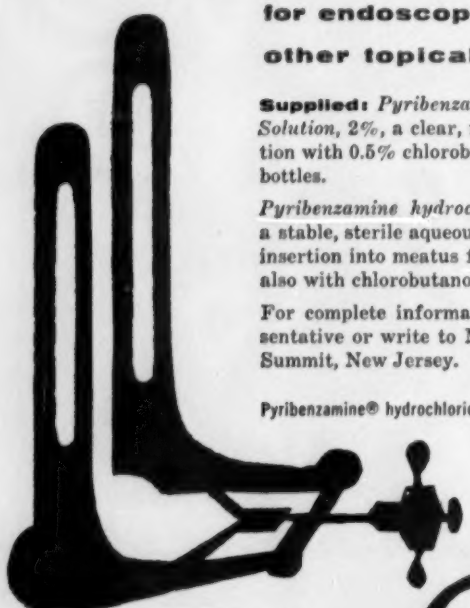

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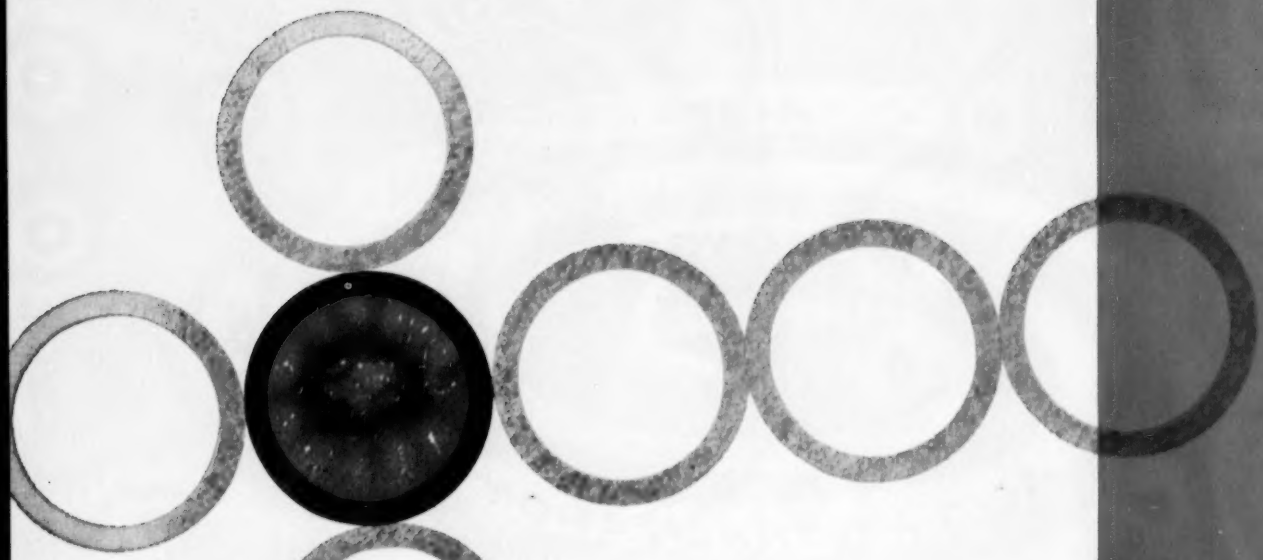

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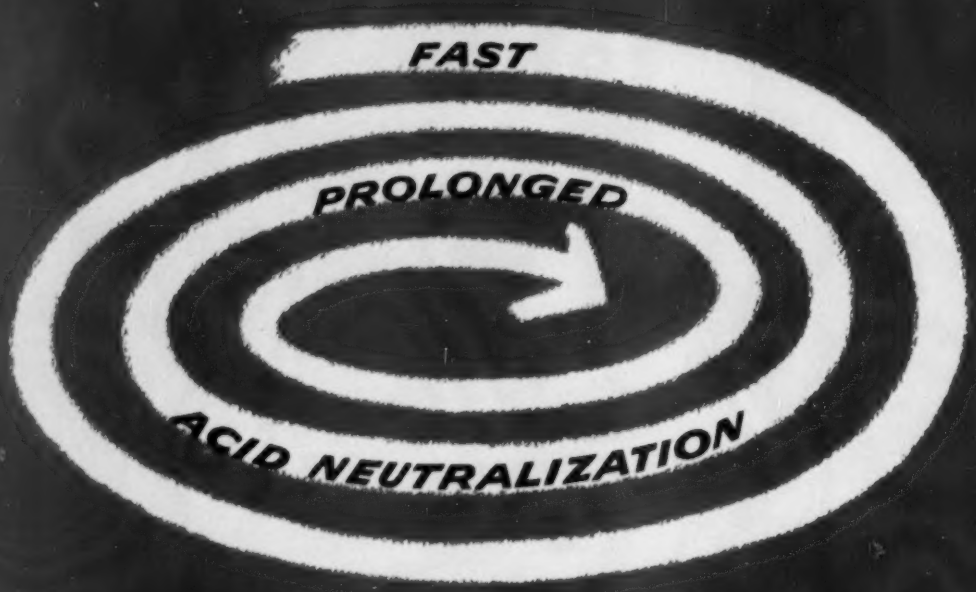

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INVESTIGATION OF ENTERIC INFECTIONS IN THE CARIBBEAN AREA*: IV. ENDAMOEBA HISTOLYTICA AND OTHER INTESTINAL PROTOZOA IN JAMAICA, BRITISH WEST INDIES

VIOLA MAE YOUNG, PH.D.,[1] OSCAR FELSENFELD, M.D.[2] AND LOUIS S. GRANT, M.D.[3]

DYSENTERIC disorders continue to have a high morbidity rate on the island of Jamaica and are the cause of a great many deaths among infants and children. Many of the agents capable of initiating gastro-intestinal disturbances have been carefully studied and campaigns against them are being waged by the island authorities. An effective anti-typhoid vaccination program is being carried out. Other Salmonella infections have been recognized and their epidemiology was studied and reported in the second section of these investigations (1). Helminths are known to be a serious problem and great strides have been made in the eradication of hookworm.

The role played by the intestinal protozoa in gastro-intestinal disturbances on the island, however, has never been carefully scrutinized. The present study was undertaken to help clarify the position of the intestinal protozoa in these diseases as a fourth part of the inquiry into the cause of diarrhea in the Carribean area.

To make the survey as complete as possible, fecal specimens were collected from a number of different sources, i.e., from adults and from children with and without diarrhea, from urban and provincial hospitals, from university students and young school children, and from charity institutions and contacts of positive cases.

The largest amount of material from adults with diarrhea was obtained from the Kingston area which is inhabited by about 130,000 persons of chiefly African, East Indian and Chinese descent. Both private physicians and the Kingston General Hospital cooperated in making this material available. Diarrheal specimens from adults were also obtained from several provincial hospitals. These same sources, together with the Child Welfare Association Clinic, provided the stools for examination from children with diarrheas.

Surveys were run on school children from the Kingston area, the south sea shore and the higher midlands. Material from 50 young adults, who were students and nurses, was obtained through the University College of the West Indies. Further surveys were run on the inmates of prison farms and almshouses.

*This is one of several papers reporting the findings of a survey party sent out by the Tropical Research Foundation and by the Lasdon Foundation to study enteric disease in the Carribean area.

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Lastly, a number of examinations were made on persons who were contacts of proven cases of infection with *Endamoeba histolytica*. Most of these contacts were the members of the families of school children.

METHOD

The fecal specimens were collected directly into bottles containing 10% formalin to prevent degenerative changes during transport to the laboratory. Wet smears were made directly of the formolized stool and also with D'Antoni's iodine (2). In case there was difficulty in identification of protozoa present in the specimen, permanent hematoxylin stained smears were prepared with a modified Ratcliffe and Parkins method (3,4). From one to three specimens were run on each patient as it was impossible to obtain repeat specimens in many instances.

RESULTS

A total of 2,591 persons submitted fecal specimens for examination. Approximately 27% yielded *Endamoeba histolytica*, 41% *Endamoeba coli*, 43% *Endolimax nana*, 5% *Iodamoeba butschlii*, 0.6% *Dientamoeba fragilis*, 14% *Giardia lamblia*, 3% *Chilomastix mesnili* and 0.5% *Trichomonas hominis*.

Table I shows the percentages of positive findings for intestinal protozoa from the adults together with the source of the specimens. The patients of private physicians, Kingston General Hospital patients and the provincial hospital patients all had diarrhea. The students and nurses from the University Hospital and the prison farm and almshouse inmates did not, though it is impossible to assume that these latter were completely symptomless. The highest infection rate for *E. histolytica*, 27.4%, occurred in specimens submitted by private physicians, undoubtedly accounted for by the careful selection of cases from which specimens were sent. Kingston General Hospital, at the time the survey was carried out, was receiving a number of patients with bacillary dysentery which could provide an explanation for the low percentage of positive *E. histolytica* findings. The great fluctuation in percentages of the findings of the various intestinal protozoa from specimens received from the prison farms and almshouses is not surprising in view of the limited sanitary facilities and closed populations.

Table II presents the percentage of positive findings of intestinal protozoa found in the fecal specimens of infants and children submitted from various sources. Many of the specimens from the Child Welfare Association Clinic and private physicians were collected from infants, while those from the provincial hospital were largely from children above two years of age. The non-

TABLE I

NUMBER AND PERCENT OF INTESTINAL PROTOZOA FOUND IN JAMAICAN ADULTS

Source		E. histolytica	E. nana	E. coli	I. butschlii	D. fragilis	G. lamblia	C. mesnili	T. hominis	Total Number Examined
Diarrhea present										
Private	#	105	137	221	21	2	27	12	3	383
Physicians	%	27.4	35.8	57.7	5.5	0.5	7.0	3.1	0.8	
Kingston	#	23	67	42	11	1	38	15	1	193
Hospital	%	12.0	34.7	21.8	5.7	0.5	19.7	7.8	0.5	
Provincial	#	49	102	150	37	2	51	12	2	219
Hospital	%	22.4	46.6	68.5	16.9	0.9	23.3	5.5	0.9	
Normal specimens										
Students and	#	10	27	18	5	1	4	1	1	50
Nurses	%	20.0	54.0	36.0	10.0	2.0	8.0	2.0	2.0	
Prison	#	7	11	24	1	1	19	0	0	37
Farm	%	18.9	29.7	64.9	2.7	2.7	51.4	0	0	
Almhouse	#	34	103	57	2	0	21	19	1	157
	%	21.7	65.6	36.3	1.3	0	13.4	12.1	0.6	

diarrheic specimens were all collected from children of school age. The number of specimens from infants with diarrhea submitted from the Kingston General Hospital was so small that the percentages cannot be considered valid and were not included in the final calculations.

The contacts of cases positive for *E. histolytica* were comprised of both children and adults, but were included in Table II for the convenience of comparison. The high infection rate, 36.1%, of *E. histolytica* from the provincial hospital probably indicates that the patients were drawn from a highly endemic area. It should be pointed out that simultaneous bacteriologic

TABLE II

NUMBER AND PERCENT OF INTESTINAL PROTOZOA FOUND IN JAMAICAN CHILDREN AND CONTACTS

Source		E. histolytica	E. nana	E. coli	I. butschlii	D. fragilis	G. lamblia	C. mesnili	T. hominis	Total Number Examined
Diarrhea present										
Private	#	5	9	31	5	1	10	7	1	43
Physicians	%	11.6	20.9	72.1	11.6	2.3	23.2	16.3	2.3	
Kingston	#	1	1	1	2	2	1	1	0	5
Hospital	%	20.0	20.0	20.0	40.0	20.0	20.0	20.0	0	
Provincial	#	13	10	16	1	0	0	0	0	36
Hospital	%	36.1	27.8	44.4	2.8	0	0	0	0	
Child Welfare	#	18	31	65	7	1	43	5	2	188
Clinic	%	9.6	16.5	34.6	3.7	0.5	22.9	2.7	1.1	
Normal specimens										
Kingston	#	122	236	212	17	2	43	5	1	486
Area	%	25.1	48.6	43.6	3.5	0.4	8.8	1.0	0.2	
South Sea	#	25	53	40	5	2	42	3	2	105
Shore	%	23.8	50.5	38.1	4.8	1.9	40.0	2.9	1.9	
Midlands	#	19	40	32	2	0	21	1	0	118
	%	16.1	33.9	27.1	1.7	0	17.8	0.8	0	
Contacts	#	275	233	192	19	2	48	2	0	571
	%	48.1	40.8	33.6	3.3	0.3	8.4	0.3	0	

*Balantidium coli found in one specimen.

cultures for bacillary dysentery on the specimens received from the Child Welfare Clinic revealed a high infection rate with shigella, which might well provide an explanation for the low percentage of positive *E. histolytica* findings. It is obvious that children of school age have already reached an infection rate approximately as high as the adult population. It can be noted too that school children from the higher midlands tend to be less heavily infected with intestinal protozoa than those from the south sea shore or the heavily populated Kingston area. It is not a new observation that the contacts of children infected with *Endamoeba histolytica* have generally a very high infection rate, and it was clearly borne out by the percentage of positives in this survey, 48.1%. Balantidium coli was found in one specimen from the south sea shore.

Discussion

The lack of a clearly defined difference in the percentage of positive findings from the diarrheic and non-diarrheic specimens is somewhat surprising. Before conclusions can be drawn from such findings, however, certain facts must be borne in mind. Discussions with private physicians revealed that they felt the diarrheal patients with positive findings for *E. histolytica* and negative findings for bacterial agents, frequently responded well enough to antiamoebic therapy to convince them of the need for treatment. This was particularly true for children. To assume that the specimens which were called "normal" actually came from symptomless persons would be a mistake, for the interpretation of "normal", in an area where various stages of malnutrition and subclinical disease is frequent is hazardous indeed. The contribution of such parasitism to the all-over pattern of disease is difficult to ascertain. It is surely true, however, that the infection rate is high and the symptoms comparatively light.

It should also be remembered that the true infection rate is higher than here reported. 10% formalin is a preservative of considerable value and availability, but fresh specimens or the "MIF" technique (5) would surely have given a higher percentage of positive findings. Repeated examinations and the addition of concentration techniques would have had the same effect of increasing the percentages.

Acknowledgement

Gratitude must be expressed to cooperating doctors of the government medical service and private physicians who made these studies possible. Our thanks particularly are due to Dr. Sidney Ferreira, Assistant Director of Medical Services in Jamaica, who gave every possible assistance and to Miss Linda Bryant who worked with us on the project.

Summary

A survey for intestinal protozoa was run in Jamaica, British West Indies. A total of 2,591 specimens were examined, 27% of which yielded *E. histolytica*, 41% *E. coli*, 43% *E. nana*, 5% *I. butschlii* and 14% *G. lamblia*. The findings are briefly discussed in connection with the source of specimens.

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MORPHOLOGICAL STUDY OF ABDOMINAL GAS SHADOWS

Samuel L. Beranbaum, M.D. and Kakarla Subbarao M.B., B.S.,* New York, N. Y.

THE PRESENCE of gas in the alimentary tract serves as an excellent contrast medium bestowed by nature for a critical analysis of the anatomical, physiological and pathological status of the gastrointestinal tract.

The abnormalities that are usually noted are those secondary to obstructive processes or displacement by unusual masses. In intestinal obstruction, mechanical or paralytic, the roentgenological manifestations have been well documented. Likewise, displacement of gaseous shadows by enlarged abdominal viscera or abnormal masses is well known. On the other hand, the importance of considering gas as a contrast substance for morphological study in normal and abnormal states has been neglected.

Usually, gas is considered to be a hindrance, obscuring the details of the radiological examination of the abdomen. There has been considerable increase in the requests for scout films of the abdomen before any contrast material is used. A careful perusal and critical analysis of these gas shadows will be quite rewarding, even though the films are intended for some other purpose, such as a fracture of the spine, calculus in the urinary tract or a routine film of the chest.

Under such circumstances an abdominal gas pattern from a single film may be misleading and must be approached with caution and skepticism. But an examination which requires more than one film and re-

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*Picker Foundation Fellowship as recommended by the National Research Council—Radiological Committee.

1A

1B

Fig. 1. Case 1—Carcinoma of pars cardia. A.F. A chest film illustrating a filling defect in the magenblasse. An oral barium study proved this to be an intrinsic gastric neoplasm. Pathological diagnosis was adenocarcinoma of the stomach.

2A

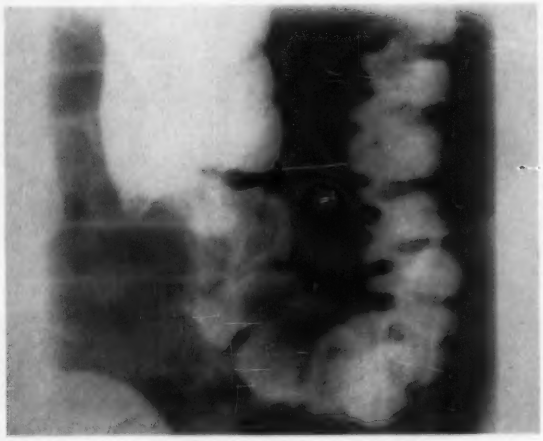
2B

Fig. 2. Case 2.—Lesser curvature ulcer of pars media. B.F., a 60-year-old woman examined for fracture of the ribs, exhibited a gas distended stomach with a shallow incisura on multiple films. Barium meal study was recommended which revealed an ulcer on the lesser curvature of pars media. The patient ultimately came to surgery and the pathological diagnosis was benign gastric ulcer.

Fig. 3. Case 3—Carcinoma of pars media. H. Z., a 70-year-old white female, admitted for retrograde pyelography. Multiple films showed a gas distended stomach with a broad incisura in pars media. Because of this abnormality, a gastro-intestinal series was recommended but the patient refused further study. She was later admitted to another hospital where the diagnosis of carcinoma of the stomach was established (personal communication by Dr. John Silberblatt).

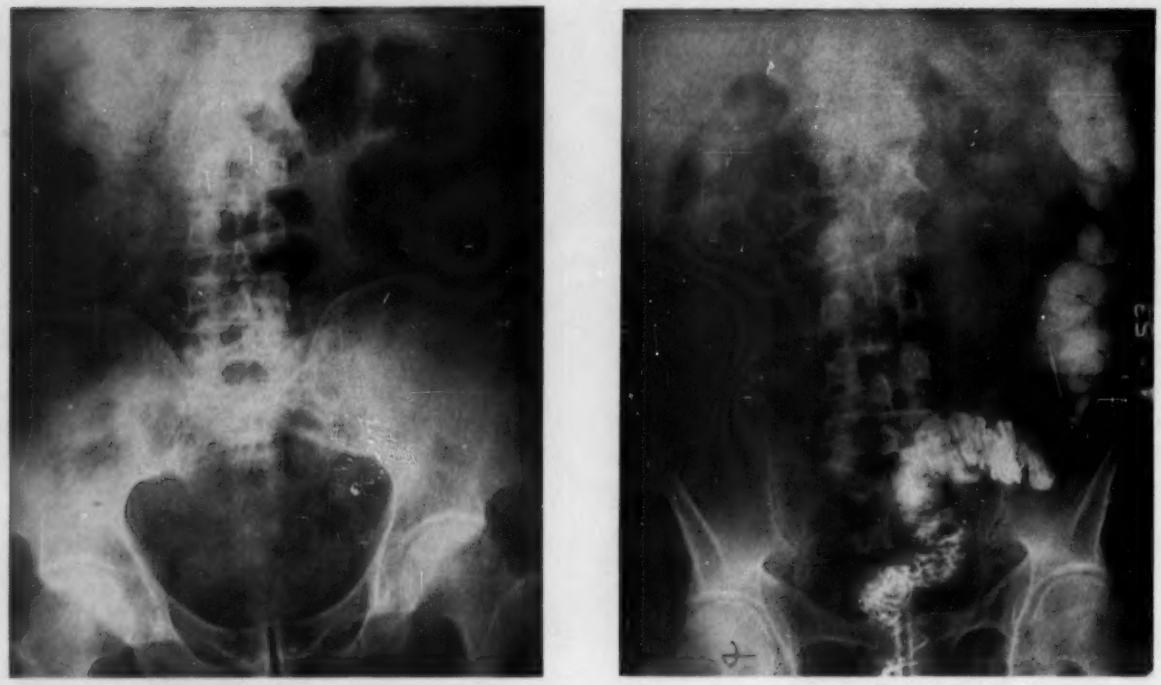
4A

4B



4C

Fig. 4 Case 4—Carcinoma of sigmoid. I. S., a 62-year-old white male admitted for urinary tract investigation which eventually proved to be a cyst of the left kidney. Multiple exposures, taken during retrograde pyelography revealed a filling defect with narrowed canalization at the proximal portion of the sigmoid which was confirmed by the barium enema examination. Pathological diagnosis was adenocarcinoma of the sigmoid.



5A 5B

Fig. 5. Case 5—Regional hyperplastic colitis. J. G., a 59-year-old white male with history of obstipation and melena. An annular filling defect with narrowed canalization of the descending colon was noted and confirmed by barium enema. Pathological diagnosis was segmental chronic hyperplastic colitis.

Fig. 6. Case 6. Pericecal hematoma. E. W., a 25-year-old white female admitted for appendectomy. On the fifth postoperative day, she developed pain in the right lower quadrant, abdominal distension and fever, for which reason scout films of the abdomen were taken, on the ninth postoperative day. An extrinsic pressure defect was noted on the lateral aspect of the gas distended cecum. At operation, it was found to be a large hematoma displacing the cecum.

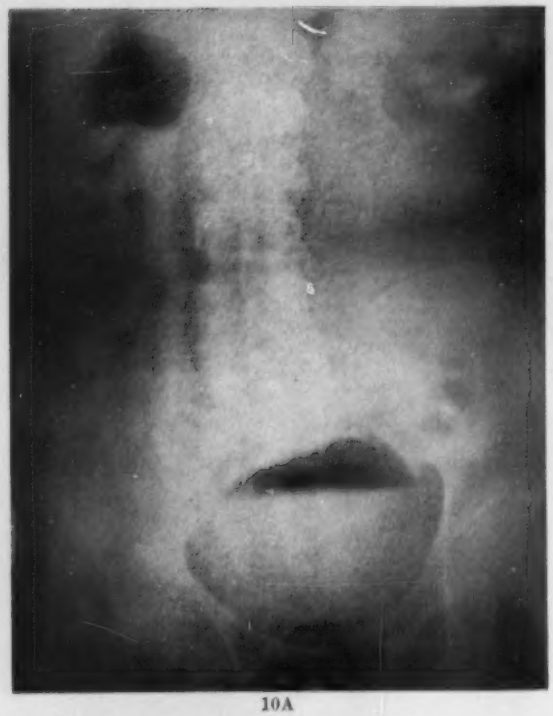
7A

7B

Fig. 7. Case 7. Appendiceal abscess. M. M., a 57-year-old white female admitted with the right lower quadrant pain and vomiting of a few days' duration. Scout films of the abdomen revealed an extrinsic pressure defect on the lateral aspect of the gas distended cecum. The roentgenological diagnosis of appendiceal abscess was established at operation.

Fig. 8. Case 8. Perinephritic abscess. C. B., a 49-year-old white female admitted with right upper quadrant pain. Scout films of the abdomen revealed a large density causing extrinsic pressure defect on the medial aspect of the ascending colon. At operation, a right perinephritic abscess was found.

Fig. 9. Case 9.—Inguinal hernia. G. M., a 59-year-old white female admitted with a history of trauma of a few hours' duration. Examination of the pelvis showed multiple fractures. A large collection of gas distended ileum was noted below the right inguinal ligament which is due to an inguinal hernia.



10A

10B

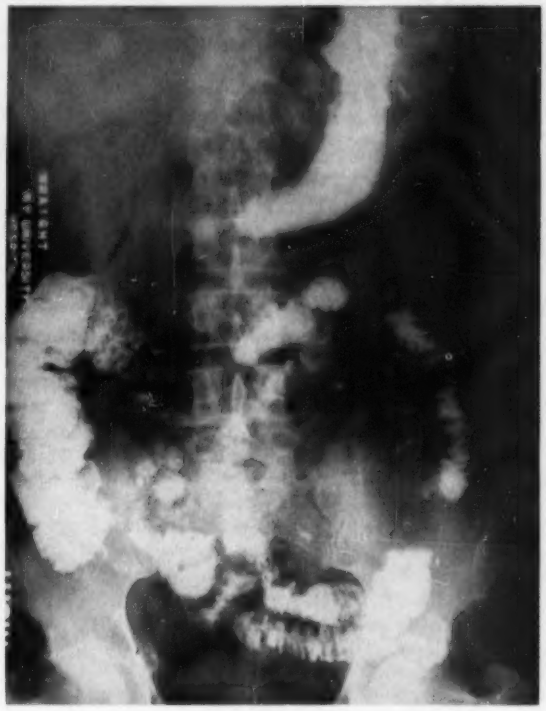
Fig. 10. Case 10.—Fistulous communication between urinary and gastrointestinal tracts. I. C., an elderly male admitted for urinary tract disease. I.V.P. revealed a hydronephrosis and hydroureter on the right side with a mixture of gas and fluid in the right collecting system and in the urinary bladder, but not in the left collecting system. The patient was not diabetic and there were no clinical signs of gas bacillus infection. A diagnosis of a fistula between the urinary and gastrointestinal tracts was made. Unfortunately, the patient refused further work-up and left the hospital.

11A

11B

Fig. 11. Case 11.—Fistulous communication between biliary and gastrointestinal tract. M. K., a 72-year-old white female, admitted with biliary colic and vomiting of two days' duration. Scout films revealed evidence of small intestinal obstruction. Gas was noted in the biliary tree. There was no evidence of radiopaque gallstone. A diagnosis of gall stone ileus was made and established surgically.

12A



12B

Fig. 12. Case 12.—Pneumocholecystitis. G. W., a 56-year-old white male who had a cataract operation two days prior to admission, with a complaint of right lower abdominal pain, distension, vomiting. A gastro-intestinal series revealed abnormal gas shadows in the wall of the gallbladder, within the lumen of the gallbladder and in the biliary ducts. Note the air fluid levels in the gall bladder and the bile ducts. The patient refused surgery. Obviously, the gas was formed by a gas bacillus infection of the gall bladder.

veals a persistent defect or abnormality is highly significant, and should be further investigated.

The normal position and morphology of the gastro-intestinal tract as outlined by gas may be altered in several ways.

A. Gas shadows revealing an intrusional mass.
   Case 1—Carcinoma of pars cardia.

B. Gas shadows with abnormal persistent incisura.
   Case 2—Lesser curvature ulcer of pars media.
   Case 3—Carcinoma of pars media.

C. Gas shadows revealing filling defect with luminal narrowing.
   Case 4—Carcinoma of sigmoid.
   Case 5—Regional hyperplastic colitis of the descending colon.

D. Gas shadows with extrinsic defects.
   Case 6—Pericecal hematoma.
   Case 7—Appendiceal abscess.
   Case 8—Perinephritic abscess.

E. Gas shadows in unusual locations.
   Case 9—Inguinal hernia.

F. Gas shadows outside the alimentary tract.
   a) Fistulae
      Case 10—Fistulous communication between urinary and gastro-intestinal tracts.
      Case 11—Fistulous communication between biliary and gastro-intestinal tracts.
   b) Gas forming organisms.
      Case 12—Pneumocholecystitis.

CONCLUSION

The importance of studying incidental gas shadows in the abdomen from a morphological point of view is illustrated.

The authors wish to express their appreciation to Dr. Maxwell H. Poppel, Professor of Radiology, New York University, for his valuable stimulation, advice and suggestions.

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EVALUATION OF CLINICAL METHODS IN GASTROINTESTINAL DISEASES. VII. TUBELESS DETECTION OF GASTRIC ACIDITY USING AN AZURE A ION-EXCHANGE INDICATOR

A. Allen Goldbloom, M. D.; Marcus A. Feinstein, M. D.; Harold B. Eiber, M. D. New York, N. Y.

THE REAL value of gastric analysis for the physician is the knowledge that a stomach can or cannot secrete acid. In the earlier days clinicians considered that hyperacidity and hypersecretion were integral parts of peptic ulcer, and, therefore, regarded the study of the gastric secretion and an estimation of degree of gastric acidity as indispensable in diagnosis (1). However, many clinicians today have begun to doubt the importance of such an examination since the acidity and quantity of the secretions are normal in many cases of ulcers, whereas in others subacidity is present and in exceptional instances anacidity has been encountered (2,3). Too much importance need not be placed on a high acid titer or on a low one; the important thing is the presence of acid (4). Greater importance should be considered to the achlorhydria after histamine (5). The test for achlorhydria is extremely valuable in the diagnosis of pernicious anemia, cancer of the stomach, and gastric polyps. The finding of achlorhydria never constitutes a final diagnosis of these conditions, but is very commonly associated with them. A simple clinical test for gastric acidity however remains indispensable.

The Difficulties of Intubation Method.

Generally, gastric analysis implies the study of gastric contents obtained through a tube. One realizes that this procedure is time consuming, unpleasant to the patient, and not always feasible. One encounters a severe psychological reaction to the introduction of the tube. With the more prolonged years of life, the patient may possess conditions which make such a procedure difficult or even contraindicated, such as asthma, emphysema, hypertension, or cerebral-vascular accidents. The passing of a stomach tube presents special problems in non-cooperative, suspicious, restless geriatric patients. One should welcome any technique which offers information regarding gastric secretion without the difficulties mentioned above, inherent in intubation. Tubeless gastric analysis is such a simple procedure (6,7,8).

Rational of Tubeless Gastric Acidity Determination

Tubeless gastric analysis has proven a simple, effective technique affording results comparable in accuracy to those obtained in the analysis of gastric samples removed by intubation (9,10,11,12,13,). Distress to the patient and alterations in composition of the gastric juice, commonly associated with intubation, have been eliminated. The tubeless procedure has been till now proven successful with an ion exchange resin compound containing quinine as the indicator cation* (14,15,16). This compound has been synthesized by combining a cation exchange resin with the indicator material so that indicator ions displace the hydrogen ions of the resin. With the introduction of this compound into the stomach, the reaction is reversed. The indicator ions of the compound are then displaced by the hydrogen ions of free gastric hydrochloric acid and excreted in the urine where their presence can be detected.

Carboxylic Resin Indicator Compound with Azure A. (Diagnex Improved)

Indicator exchange compounds with dyes such as methylene blue allow for a simple visual means of quantitation. The use of such dyes avoids the more complex quinine analytical procedure and special equipment (17,18). Segal and his associates (19) demonstrated by means of spectrophotometry, that commercially available methylene blue contained considerable quantities of the dye azure A and that dilute hydrochloric acid, in vitro, preferentially displaced the azure A from the methylene blue resin compounds. They found that, in vivo, free gastric hydrochloric acid led to the preferential excretion in the urine of the azure A present in the methylene blue compound. Therefore, Azure A has replaced quinine as the indicator cation. The new substance now used is Azure A carboxylic resin indicator compound. (Diagnex Improved). These determinations involve a simple displacement of the azure A of the indicator resin by the hydrogen ions of the free hydrochloric acid of the stomach. The presence or absence of azure A in the urine indicates the presence or absence of free hydrochloric acid in the stomach. It cannot be used to demonstrate quantitative variations in amount of free acid known to occur clinically. Estimation of the Azure A excreted makes possible the

TABLE I.

DIFFERENCE BETWEEN TUBELESS AND INTUBATION METHODS FOR ACIDITY DETERMINATION

Results	Number of Patients Tubeless Method	Intubation Method	Percentage
Negative	14	14	100
Positive	26	26	100
Total Number	40	40	—

The New York Medical College-Metropolitan Medical Center (Bird S. Coler Hospital Division).

The Carboxylic Resin Indicator Compound with Azure A used in this study was generously supplied by the Squibb Institute for Medical Research, New Brunswick, N. J. It is designated as "Diagnex Improved."

Aided by a grant from the Sophie D. Cohen and W. W. Cohen Foundation.

*Manufactured under the trade name of "Diagnex."

determination of gastric acidity by a gross visible method of quantitation. This does not depend upon special equipment nor quinine analytical procedure.

CLINICAL MATERIAL

This report represents a study of forty male and female patients in whom gastric acidity was determined by both the new tubeless and the conventional intubation methods. These patients, in addition, had roentgenological and clinical evaluation of the gastro-intestinal tract.

METHOD OF PROCEDURE

All medications such as steroid compounds, vitamin preparations, and sedatives are omitted on the day preceding the test. No food is permitted after midnight till the end of the test. On arising, the patient is instructed to urinate and discard the specimen. A capsule containing 250 mg. of caffeine sodium benzoate is given, followed by a glass of water, coffee, or tea without cream, milk or sugar. One hour later the patient voids and the entire quantity of urine collected is marked as *"control urine."* A granular mixture of 2.0 gm. of the azure A resin compound (Diagnex Improved) is emptied into a glass of water stirred well, and drunk by the patient. Urine is collected two hours after taking the azure A resin compound. The specimen is marked "2 *Hour Sample."* No urine is collected after the 2 hour period. Gastric analysis intubation was performed on another day.

TECHNIQUE OF ANALYSIS OF TUBELESS METHOD

The two hour specimen of urine collected after the administration of the azure A resin is diluted with water to 300 ml. If the volume is greater than 300 ml., the total volume is measured. The *"control"* specimen is diluted with enough water to approximate the specific gravity of the diluted test urine. Ten cc. of each of these diluted specimens are poured into test tubes and their blue color is compared with appropriate standards. A stock solution of 0.01 per cent of azure A (10 mgm. of the azure A granules per 100cc.) is prepared. This can be kept at least six months. The two comparator standard solutions are prepared from the 0.01 per cent stock solution every three weeks,—corresponding to 0.6 mg. of azure A per 300 ml and the other to 0.3 mg. of azure A per 300 ml. *The greenish tinge in the color of the 2 hour urine by inspection denotes the presence of free gastric hydrochloric acid in most instances. No other procedure need be required.* The "control" urine should be non-greenish in color. The intensity or paleness of the greenish tinged urine may be evidence of hyper- or hypoacidity. It does not imply the quantitative amount of gastric acidity. Generally, a blue color more intense than 0.6 mg. standard demonstrates the presence of free gastric hydrochloric acid. If the color is less intense than the 0.6 mg. per 300 ml. standard, both the control and the test urines are acidified with a few drops of concentrated hydrochloric acid. These tubes are placed in a boiling water bath for 10 to 15 minutes, then allowed to cool slowly to room temperature and examined for blue color as previously. The boiling procedure serves to change any colorless conjugated form of azure A that may be present in the urine to free azure A. Boiling may cause a temporary fading of the blue or green color in the urine. The color returns after 10 minutes of cooling at room temperature. The urine should be acidified before storing, if the test can not be analyzed the same day the urines are collected.

TABLE II

PRESENCE AND ABSENCE OF ACIDITY BY THE TUBELESS METHOD, CLINICALLY AND ROENTGENOLOGICALLY

Tubeless Method for Acidity	Total Number of Patients	Percentage
	Clinical	
Positive	26	65
Negative	14	35
	Roentgenological	
Positive	26	65
Negative	14	35

RESULTS OF STUDY

Forty patients, including twenty-four males and sixteen females, age 32 to 94 are included in the present study. There were twelve "normal" subjects in the older age group from the Bird S. Coler Memorial Hospital, an institution for chronic disease, with no known malignant and active tuberculous conditions admitted. Many are institutionalized for custodial care. The other patients were from the office practice of one of us (A.A.G.). Twenty-six patients (65%) revealed a positive acidity and fourteen (35%) absence of acidity by the tubeless method. Similar results were obtained by the intubation method. There is no difference in results between the tubeless and intubation methods for acidity determinations, producing a 100% effect (Table I).

In the patients x-rayed twenty-six (65%) showed positive acidity, fourteen (35%) revealed negative acidity by the tubeless method. The clinical, roentgenological, and gastric analytical studies were in agreement. (Table II).

There appears to be no characteristic gastric acidity values for the varied age groups. In the 40-49 year age group, the average acidity value was less than that en-

TABLE III

AVERAGE GASTRIC ACIDITY VALUE IN UNITS BY INTUBATION METHOD IN VARIED AGE GROUPS

Age Group Years	Number of Patients	*Gastric Acidity (Average)* Free (Units)	Total
30-39	5	41	68
40-49	5	20	39
50-59	9	43	65
60-69	6	27	49
70-79	7	7	22
80-89	5	11	20
90-95	3	3	16
Sex			
Male	24	23	41
Female	16	27	47
Total	40		

countered in the other middle age individuals. Hypoacidity is prevalent in the older age groups, from 70 to 95. The average gastric acidity was practically the same for the male and the female sexes. (Table III).

The gastro-intestinal conditions encountered by roentgenological studies revealed no malignancy. Absence of gastric acidity by the tubeless method was noted in varied states. (Table IV).

Of the fourteen patients presenting no acidity, under the x-ray group, twelve were encountered in "normal" geriatric individuals, with the following x-ray diagnoses: Normal roentgenological diagnosis (10); prolapse gastric mucosae (1); hiatus hernia (1). Two patients were of the middle aged group. One post-operative stomach was encountered in a male adult, who had no acidity pre-operatively for a Hodgkins disease of the stomach. The prolapse gastric mucosa (1) in the other middle aged male showing absence of acidity was due to the severe vomiting while partaking of the ion exchange resin indicator. This was the only incidence of vomiting in the series. It was a coincidental condition, not due to the resin indicator, but a gall bladder attack. Surgery later revealed gall stones in this patient. Acidity was found in the cases of duodenal ulcer and prolapse gastric mucosae (Table IV).

DISCUSSION

With the greater number of population attaining and living a healthy life beyond the age of 60 and 70, and with a large number of geriatric patients in our practice, one encounters medical conditions which contraindicate gastric acidity determinations by intubation. Tubeless gastric analysis has been shown to be a simple procedure for revealing the presence or absence of gastric acidity. It makes it possible to screen large numbers of patients and eliminate unnecessary x-ray examinations in older individuals. Our previous studies by the tubeless method (14,15) showed a greater frequency of achlorhydria (30 per cent in normal geriatric subjects) than others observed (20, 21). Debilitation, marked anemia, malnutrition, and progressive gastritis were not present in our geriatric patients to account for the achlorhydria as reported by others (22,23).

TABLE IV

GASTROINTESTINAL CONDITIONS STUDIED BY X-RAY SERIES WITH THE PRESENCE OR ABSENCE OF GASTRIC ACIDITY BY THE TUBELESS METHOD

X-ray Diagnosis	Number Patients	Tubeless Method For Acidity Determination	
		Positive	*Negative*
NORMAL	15	5	10
Diverticulosis of Colon	1	1	—
Duodenal Diverticulum	1	1	—
Duodenal Ulcer	6	6	—
Hiatus Hernia	1	—	1
Post-operative Stomach	2	1	1
Ptosed Stomach	1	1	—
Prolapse gastric Mucosae	11	9	2
Spasm Pylorus	2	2	—
Total	40	26	14

Discrepancy between the negative tubeless gastric acidity method and the positive intubation for acidity was 11.1 percent with the older preparation of Diagnex (14,15). There was a 100 per cent correlation with the present new ion-exchange resin compound with azure A. *Simplicity of the procedure and determination; the frequency of obtaining gastric acidity by the tubeless method as with intubation; and the feasibility warrant this technique to be used by the physician.* There are no contraindications to this method except when dealing with conditions which may prevent the azure A indicator to be excreted by the kidneys, such as severe renal disease, hepatic and pyloric obstructions.

CONCLUSIONS

1. Acidity determinations were studied in male and female individuals, from ages 32 to 94.

2. Two procedures (for gastric acidity) were performed, the intubation and the tubeless.

3. Clinical and roentgenological studies corroborated the gastric acidity findings.

4. There was no discrepancy in ascertaining gastric acidity by the tubeless or intubation methods. There was 100 per cent correlation.

5. The absence of acidity was mostly noted in normal geriatric individuals.

6. There appears to be no characteristic gastric acidity values for the varied age groups.

7. Hypoacidity evident in our older age group is not due to debilitation, marked anemia, malnutrition, nor progressive gastritis.

8. The tubeless method for gastric acidity by the carboxylic resin indicator with azure A (Diagnex improved) is a simple procedure. It can be carried out in the physician's office without any special apparatus or technical help.

9. This technique for tubeless gastric acidity is advocated to be used by the physician for routine and screening purposes.

ACKNOWLEDGMENT

The authors are grateful to Drs. A. Dale Console and Marshall I. Hewitt of the Squibb Institute for Medical Research for their interest and generous supply of the Carboxylic Resin compound with Azure A; to Dr. Robert Coleman Batterman for permission to study the patients on his service; to Dr. Edmond G. Hadra, for aid in the supervision; to Mrs. Margaret Doyle, charge nurse, for her cooperation; to our secretary Miss Zelda Forman.

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PEPTIC ULCER IN LAENNEC'S CIRRHOSIS*

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THE HIGH incidence of peptic ulcer in Laennec's cirrhosis needs further emphasis. Some have considered the combination so rare as to justify publication as a case report (1,2). De La Cruz (3) in 1950 found 11.8 per cent of the patients with cirrhosis of the liver had peptic ulcer proven on x-ray. Antonini and Marinoni (4) in 142 autopsied cases of Laennec's cirrhosis of the liver found a five per cent incidence of peptic ulcer. Tipp and Lipsitz (5) in 130 cases of Laennec's cirrhosis coming to autopsy found 11.5 per cent with peptic ulcer while hyperemic gastritis, with or without petechial hemorrhages, was found in 33 per cent. Other investigators (6,7,8,10) have found an incidence of 1.8 to 25 per cent of peptic ulcers in Laennec's cirrhosis. The average figure is about nine per cent. It is of interest that surgical lesions of the biliary tract have also been accompanied by an increased incidence of peptic ulceration.

Method: Four hundred and seventeen patients with Laennec's cirrhosis were studied over a period of four to five years, among other things for signs of peptic ulceration. All patients were personally examined by one of the authors (H.D.B.). Only definite roentgen evidence of peptic ulceration was accepted as establishing a diagnosis of peptic ulcer. Those patients with typical symptoms but no x-ray evidence of peptic ulcer were counted as not having peptic ulcer. Only patients suffering from severe cirrhosis, the complications of cirrhosis, or other unrelated disease were admitted to the hospital and hence examined. This may well alter the statistical findings, perhaps making this report better headed "Peptic Ulcer in Laennec's Cirrhosis Among Hospitalized Patients." For reasons of brevity the present title was chosen.

Results: Of 417 patients with Laennec's cirrhosis (as determined by the criteria of abnormal liver function, hepatomegaly, liver biopsy in 67 cases, and alcoholism), 58, or 13.9 per cent, had x-ray proven peptic ulcer in addition to their liver disease. Fifty-one had duodenal ulcers, one of these having a concomitant gastric ulcer. Seven patients had only gastric ulcers.

X-ray evidence of duodenal ulcer was found in 47 cases. Postmortem examination revealed one healed duodenal ulcer and three active duodenal ulcers not demonstrated by x-ray studies.

Gastric ulcer was diagnosed in six cases by roentgen demonstration while one other not demonstrated during roentgen studies of the upper gastrointestinal tract was demonstrated on autopsy.

A good ulcer-type history of epigastric pain relieved by food or alkalis was obtained in only 15, or 30 per cent, of the patients who were found to have duodenal ulcer. Five patients with gastric ulcer, or 62 per cent, gave a typical ulcer story. As most of the cases used alcohol excessively, it was not surprising that a common complaint was constant abdominal pain unrelieved by alkali or food.

Gastric analysis in these patients with Laennec's cirrhosis and ulcer was essentially as reported for patients without cirrhosis who have ulcer, in that the

*From Veterans Administration Hospital, Hines, Illinois.

duodenal ulcers ranged from 12° to 70° free hydrochloric acid, none having achlorhydria while one gastric ulcer had achlorhydria and the others had low values to a maximum of 30° free hydrochloric acid.

Serum proteins were studied in 25 patients with duodenal ulcer, 8 (32 per cent) were abnormal. In the total series 377 patients had protein determinations of which 228, or 60 per cent, were abnormal. There is an obvious discrepancy in these figures in that abnormal A/G ratios and total proteins are found two times as frequently in the group with Laennec's cirrhosis alone as compared to the group with combined ulcer and Laennec's. This was not what had been anticipated. The same sequence of events occurred in patients with gastric ulcer in that only two out of six, or 30 per cent, demonstrated abnormal proteins. The numbers involved are not considered significant figures.

Among the peptic ulcer patients, 20 were examined in detail by esophagograms and esophagoscopy for evidences of esophageal varices. Four, or 20 per cent, were found to have varices. This incidence did not differ materially from the entire series of 417 patients among whom 20 per cent were found to have esophageal varices during one of their examinations. Using splenomegaly, esophageal varices, or increased collateral abdominal circulation as signs of portal hypertension, 65 per cent with ulcer had portal hypertension but 85 per cent without ulcer had these findings.

Hyperbilirubinemia was studied as to its possible effect on peptic ulceration in patients with cirrhosis. Of the peptic ulcer group 56 per cent had hyperbilirubinemia of over 2.5 milligrams per cent whereas 242 of 348 patients with cirrhosis and no peptic ulcer had hyperbilirubinemia. This is an incidence of 68 per cent. There was no evidence that bilirubinemia when present was any more severe, or for that fact, as severe in the peptic ulcer group as compared to the group with cirrhosis alone. The highest bilirubin in the ulcer group was eight milligrams per cent. No patient with marked prolonged hyperbilirubinemia developed peptic ulcer.

Discussion: The finding of peptic ulcers in 13.9 per cent of the patients in this series is well above the expectancy for peptic ulcer in hospitalized patients (16). Alvarez (13) found an incidence of 3.3 per cent at the Mayo Clinic, while Steigmann found that .88 per cent of Cook County Hospital admissions were for peptic ulcer. Jamison found that among employees of Metropolitan Life Insurance Company, peptic ulcer had an incidence of 1.38 per cent. Drammen, in a study of 21,918 adults above 15 years of age, found that peptic ulcer was present in 2.45 per cent. Extensive studies of autopsy material give peptic ulcer incidence from one to 11 per cent, with the majority reporting around 5 per cent of all autopsies showing peptic ulcer or residual scar. There are several factors which may lead to increased incidence of peptic ulcer in cases of Laennec's cirrhosis.

The first factor to be mentioned in any statistical study is that of selection. With no exceptions these patients were male. These patients were selected in that they were given a screening examination prior to admission. This was done to determine the need for medical or hospital care. Thus the criteria for admission was either a severe cirrhosis, some complications of cirrhosis, or some other disease in addition to cirrhosis. The survey then, was limited to those cirrhotics ill enough to require hospitalization and does not represent all cirrhotics.

The physiological and pathological states present in cirrhosis may increase the predilection towards peptic ulceration. Among possible factors to be discussed below are: 1) Absence or relative absence of neutralizing bile salts from the gastro-intestinal tract. 2) Stimulatory effect of alcohol on hydrochloric acid secretion. 3) Direct inflammatory effects of alcohol on gastric and duodenal mucosa. 4) Increase of portal pressure and resultant venous stasis in bowel. 5) Malnutrition and altered serum proteins. 6) Steroid metabolism alterations; and finally 7) psychosomatic phenomena.

Because of the common coincidental finding of peptic ulcer and liver and biliary tract disease, one may be the cause and the other effect. The fact that most dogs having their bile ducts ligated for experimental work die of perforated peptic ulcer (13,14,15) lends weight to this idea. Sherwood (11) in 1928 found that in 200 cases with surgical lesions of the biliary tract 29, or 14.5 per cent, had associated gastric or duodenal ulcers. Shapiro and Lifvendahl (12) found in 15 cases of tumors of the extrahepatic bile ducts that four had active duodenal ulcers. Rivers and Mason (9), in studying peptic ulcer, found 13.6 per cent of duodenal ulcers and 7.8 per cent of gastric ulcers have associated disease of the gallbladder.

The loss or diminution of alkaline bile flow into the duodenum and its reflux into the stomach as a protective element against ulceration and a buffer to gastric acidity is an important factor. The experimental work mentioned above lends weight to this consideration. The patient with cirrhosis during his severe alcoholic intake and inadequate food intake might injure the liver cells to a point at which bile flow is less or contains less alkaline salts.

Increased hepatic bile content caused by ligation of portal vein in dogs or by injection of bile salts into the portal vein has been reported to cause a marked increase in systemic blood histamine levels reaching 35 times control levels. This potential source of strong continued stimulation to gastric secretion of hydrochloric acid might be a factor in peptic ulcer formation (18,19).

Although this hypothesis is attractive, we were unable to support it clinically in that patients with prolonged hyperbilirubinemia did not develop peptic ulceration and the incidence of hyperbilirubinemia (thence presumably exclusion of bile salts from the bowel) among patients with peptic ulcer was, if anything, less than among our controls (cirrhosis with peptic ulcer). This explanation cannot be completely eliminated but seems unlikely to be affecting this group.

Alcohol has long been used to stimulate hydrochloric acid secretion. The long continued stimulation of hydrochloric acid secretion by alcohol without the buffering action of food must be an important factor in the in-

creased incidence of peptic ulcer in cirrhotic parients. It would be possible, due to the chronicity of both diseases, for a person to develop an ulcer with elevated hydrochloric acid secretion and later develop cirrhosis of the liver with possibly a lower hydrochloric acid secretion or perhaps an achlorhydria. All of the patients with duodenal ulcer that were examined had free hydrochloric acid in the stomach at the time of examination, although the levels were not high in most cases. One patient had 44° free hydrochloric acid in 1941 while this had declined to 26° in 1951. Another in 1945 had 60° free hydrochloric acid and in 1951 this had declined to 15°.

While some have found little correlation between gastritis and alcohol, (17) others have found an increased incidence. (6). The inflammatory effect of alcohol per se on the gastric mucosa of an individual who is struggling unsuccessfully with emotional problems and is showing the effect of environmental pressures needs further study as does study of the effects of alcohol on the "protective" mucous barrier.

Portal hypertension may be a factor causing congestion of the stomach and duodenum with a lowering of tissue resistance and changes in circulation leading to ulceration in much the same manner as the varicose ulcer of the leg.

This concept fits in well with the vascular concepts of peptic ulcer. We sought for evidence to support this idea. No evidence could be found that portal hypertension was more common in patients with peptic ulcer and cirrhosis than in patients with cirrhosis alone. As a matter of fact, those patients with peptic ulcer and cirrhosis had less portal hypertension. Perhaps they were milder cirrhotics. Fluctuations in portal hypertension as previously reported may play a part (20).

Hypoproteinemia occurring in the course of liver disease and alcoholism might contribute to the lowering of tissue resistance. We were unable to confirm this hypothesis in that proteins in general were much more normal in the peptic ulcer group than in those with cirrhosis alone. This does not eliminate the possibility that the proteins had been low previously, especially when the ulcer was initially formed and had subsequently changed towards normal. Rapid changes in serum proteins were frequently observed in the course of this study.

Perhaps we should include disorders of steroid metabolism in the etiology of both Laennec's cirrhosis and peptic ulcer. The perforation of peptic ulcer under the impact of steroid therapy has been previously seen by us (21) and many others. The increase in girdle distribution of fat and the round face is seen early in many alcoholics. Then follows the spider nevi and at last the long thin nose and emaciation of the terminal patient with cirrhosis. These changes could all accompany subtle changes in steroid metabolism. We have also found an increased incidence of such diseases as asthma, rheumatoid arthritis, and gout in patients with Laennec's cirrhosis.

Alcoholic patients routinely demonstrated psychiatric disorders such as narcissistic behavior, anxiety, juvenile reactions, and had multiple psychosomatic complaints. These characteristics are often found in patients with peptic ulcer. Perhaps these basic underlying personality similarities account in part for the increased incidence of peptic ulcer in patients with cirrhosis.

It is probably a combination of factors which accounts for the increased incidence of peptic ulcer. Most important seem to be the direct stimulating and irritant action of alcohol, absence of neutralizing food, and perhaps a decrease in flow of bile salts, and finally underlying psychiatric disturbances. We could find no evidence in our series to incriminate portal hypertension, hypoproteinemia, or hyperbilirubinemia.

This study indicates that one cannot assume that hematemesis or melena in a known Laennac's cirrhosis is always due to a ruptured esophageal varix. The common coincidental finding of peptic ulcer with Laennec's cirrhosis makes it imperative that an accurate diagnosis be made as soon as possible in a patient with Laennec's cirrhosis who is bleeding from the gastrointestinal tract.

The patient who is recovering from a prolonged alcoholic episode often has nausea, vomiting, and abdominal discomfort. This may be attributed to the direct and irritating action of alcohol on the gastrointestinal tract or to the excessive preoccupation with oneself so often seen in alcoholics and no further investigation of the gastrointestinal tract done. Only when the ulcer is looked for is it found and this may explain why there is so little evidence in the literature of this common finding.

SUMMARY

In an investigation of 417 cases of Laennec's cirrhosis, peptic ulcer was found in 13.9 per cent. Of these patients with peptic ulcer 28 per cent, or 16, were admitted because of hemorrhage from the ulcer. Some of the factors leading to this increased incidence of peptic ulcer in patients with Laennec's cirrhosis are discussed.

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SCURVY IN NEBRASKA: II. THE EPIDEMIC OF SCURVY AMONG THE INDIANS OF THE OMAHA TRIBE, 1845-1846

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IN THE FIRST paper of this series (1) we gave an account of the epidemic of scurvy in the garrison at Cantonment Missouri (Fort Atkinson), situated at the present site of the village of Fort Calhoun, about sixteen miles north of Omaha, Nebraska. Of the five hundred soldiers who fell ill of scurvy, 157 died of that disease. The cause was lack of antiscorbutic foods. As these became available scurvy disappeared among the soldiers of that frontier post. The epidemic occurred in the fall and winter months of 1819-1820.

The second epidemic of scurvy in Nebraska occurred in 1845-1846 among the Omaha Indians. We first came upon these Indians as a result of the acquistion from Napoleon of the territory of Louisiana in 1803. About the time the Mormons on their trek to Utah had reached the place now known as Florence, a town that came into existence in 1853 and which was annexed to the city of Omaha in 1917, a portion of the Missouri valley, now included in southeastern Nebraska and in southwestern Iowa, had but very few white settlers. The eastern slope of the valley stretching from the Missouri River back to the lands of the Indian tribes known as the Sacs and as the Fox was occupied by the Pottawattamie Indians, about 2250 in number. The Pottawattamies and some Ottawas and Chippeways were granted by the Federal Government five million acres of land embracing a large part of what is now included in southwestern Iowa. The Pottawattamies and their allies were removed from Chicago and in time located on the newly acquired land. They came under the supervision of a government agency located in what is now Council Bluffs, Iowa. Except for a few settlements of whites near the Missouri state line, the government agency at a place now called Council Bluffs, Iowa, opposite Bellevue, Nebraska, and scattered posts of the American Fur Company, the eastern slope of the Missouri Valley was in the sole use of the Pottawattamies and their Ottawa and Chippeway allies. By a treaty made with the Federal Government on June 5, 1846, the Pottawattamies disposed of their Iowa lands, but reserved for themselves the temporary right of occupancy.

When the territory of Louisiana was acquired by the United States in 1805, the Otoe tribe was estimated to consist of 200 warriors including 25 or 30 of the Missouri tribe, who had taken refuge with them about the year 1778. The Omahas in 1799 numbered 500 warriors. Before the acquisition of Louisiana, however, in 1803, the Omahas had suffered heavy loss of life through the ravages of smallpox. Their number was still further reduced by warring with their old foes, the Sioux. Unprotected from these Indians the Federal Government nevertheless forbade them to enter a defensive alliance with other tribes. In the early part of December 1846, while the Mormons were living in their temporary abode in "Winter Quarters" at the present site of Florence, now a part of the city of Omaha, Nebraska, a war party of about a hundred Sioux warriors coming upon an encampment of the Omaha Indians, engaged in hunting buffalo and deer, some sixty or seventy miles up the Missouri River, fell upon these Indians in the dead of night and proceeded to shoot down the sleepers. In this massacre seventy-eight Omahas were killed and only a few managed to escape. (2). According to Nibley in his recent historic work, "Exodus to Greatness" (3), there were only forty-eight in the Omaha party and only eight remained alive after the bloody massacre.

In 1845, the year before the arrival of the migrating Mormons among the Omahas, scurvy developed among them, according to the historian, Hubert H. Bancroft (5), to Clyde B. Aitchison (4) and to Colonel Thomas L. Kane* (6), brother of the famous Artic explorer

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*Council Bluffs, Iowa, was first named Kanesville in honor of Colonel Kane for his kindness and assistance to the Mormons. Practically all the people at that time were unfriendly to the Mormons and displayed unwarranted prejudice against them.

and physician, Dr. Elisha Kane. It has been estimated that one-ninth of the Maha or Omaha Indians died of scurvy and its complication, intercurrent infection. None of these three writers states population figures, so that we have no idea of the actual number of natives who succumbed to scurvy.

Colonel Kane, who was in contact with the Omaha Indians around the year 1846, stated that while he was among them they were so ill-fed that their protruding high cheek bones became so prominent that they took on the appearance of a tribe of consumptives. The buffalo had left them and there were no good ranges within several hundred miles of their reach. Hardly any other game was to be found on their lands. Besides, they were very short of ammunition. Their annuity from the Federal Government was trifling. They had planted some corn in their awkward Indian fashion. Through fear of ambush they dared not venture to harvest their crops. A chief source of their food supply came from the spoilation of their neighbors, the prairie field mice. These rodents were better and wiser providers than the Indians. The little animals gathered for the winter in their underground hiding places the small black hard seeds or beans of the wood pea vine. One single mouse collected as much as a half pint before cold weather set in. The Indians robbed these collections for their own use, leaving the poor mice to starve.

The Pottawattamie tribe of Indians, living in what was at that time the territory of Iowa, and neighbors of the Omaha tribe of Indians across the Missouri River, fared somewhat better, but not too well. Their renowned chief, Pied Riche, surnamed Le Clerc, on account of his scholarship, welcomed the Mormons in the following words:

"My Mormon brethren: The Pottawattamie came sad and tired into this unhealthy Missouri Bottom, taken from his beautiful country, beyond the Mississippi, which had abundant game and timber and clear water everywhere. Now you are driven away, the same as we, from your lodges and lands there and the graves of your people. So we have both suffered. We must help one another and the Great Spirit will help us both. You are now free to cut and use all the wood you may wish. You can make all your improvements, and live on any part of our actual land not occupied by us. Because one suffers and does not deserve it, is no reason why he shall always suffer, I say. We may live to see all right yet. However, if we do not, our children will. Bonjour."**

When the Mormons met the Omahas in 1846, the latter were reduced to a miserable, poor wretched lot, a pitiable handful of scarcely more than a hundred families, the prey of disease and poverty, unlucky in the hunt, too fearful of ambush and too apathetic to venture from the shadow of their tepees to gather their scanty crops. It was this miserable condition of mind and body which no doubt prevailed in 1845 that accelerated and precipitated the onset of scurvy as a result of lack of fresh meat from the hunt and lack of antiscorbutic plant foods. The pauperized Omahas welcomed in their midst the arrival of the Mormons who could act as a buffer between the hostile Sioux and themselves and who could also help them solve their food shortage.

The third epidemic in Nebraska which was indeed a very severe one, appeared among the Mormons the year following the epidemic of scurvy among the Omaha Indians, in whose land they temporarily sojourned.

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**This speech was delivered in the French language.

VALVE AT MIDDLE OF DUODENUM

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ABOUT TWO centimeters beyond the entrance of the common bile duct, at the angle where the descending duodenum turns left to become the transverse portion, there is a well-marked, constant fold which is thicker than the usual plica circularis. It is based chiefly on the left side (mesenteric border), immediately at the angle. The duodenal tube is definitely subdivided into two portions by this valve of the middle of the duodenum. A series of the 32 duodenums retained from the regular cadaver materials of the first year medical class this year has been studied. All present the valve in one of its forms, and 18 specimens have been preserved (1).

*From The William Waldo Blackman Laboratory of Anatomy. The New York Medical College and Flower-Fifth Avenue Hospitals, New York.

The valve shows (a) a thick, ring-like (crescentic) base which continues around the duodenal lumen and becomes thinner. A sub-type (b) shows a membranous reduplication of the mucosa further decreasing the size of the lumen. This, too, is crescentic and thins out until only the thickened base remains at the anti-mesenteric border. A sub-type (c) consists of a set of two parallel valves, closely set, but between these two plicae on the pancreatic side there is seen a deep "pit" or depression. Proximal to any of the types of valve there is a longitudinal plica reaching from the area of the papilla of Vater to the transverse basal margin of the valve. This longitudinal plica seems a continuation of the longitudinal fold between the papilla minor and papilla major (Vater).

Bailey and Miller (2) state that normally the duodenum becomes closed very early in embryonic life (stenosis or atresia). Usually this closure soon disappears. Johnson, in Morris (3), describes some changes in the embryonic wall and lumen which may influence the valve here described.

At the level of the valve there are two different blood-supplies, one from the hepatic artery, and the other from the superior mesenteric. The nerves accompanying this vascular arrangement are of distinctly different origins. It may be termed a "nodal" point in the alimentary tract (4).

Clinical study, as by Shallow, Wagner and Manges (5) giving review of literature, and a special case of neoplasm as a ring around the duodenal tube in this valvular formation, indicates the difficulty of "radiologic" diagnosis, and the importance of considering the actual presence of the valve. This area is known for difficult diagnosis, see Editorial (6). The valve also complicates certain other difficulties.

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HOW TO PROVOKE AMOEBAE APPEARANCE

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IT HAPPENS sometimes that a patient presents a picture clinically suspicious of amoebiasis, while the laboratory findings, in spite of the bacteriologists's efforts, remain negative. In order to render easier the appearance of the Entamoeba histolytica in the laboratory work in such "occult" cases, we suggest the following steps:

Let the patient buy about 500 Gm. of skimmed milk powder and prepare about two days before the laboratory examination a 10% suspension of the powder in tap water, i.e. 200 Gm. in two liters of water per day; the patient can enjoy it as milk, coffee, cacao (always boiled) with or without sugar as preferred.

This drink causes a diarrhea generally on the second day of its use and if the amoebae in any form are present, they will appear in the diarrhoeic stool presented freshly on those days to the laboratory. How to explain this phenomenon? This milk acts as a laxative for 3 reasons: 1) The milk powder is prepared by heating; the lact-albumin coagulates and does not revert to its original state through dispersion in water, and the coagulated albumin irritates the intestine; additionally the casein coagulates due to the action of the acids. 2) The excess of the lactose contained in the skimmed milk powder (49.04%) acts as a laxative also. 3) The third activator (factor) is the sodium bicarbonate added during the milk powder preparation.

It may be that the skimmed powdered milk or its ingredients exercise additionally some specific action on the amoebae. In any event, the use of this simple palatable medium renders the appearance of the amoebae, if they are present in the suspected case, much easier.

EDITORIAL

WILLIAM BEAUMONT: BACKWOODS SCIENTIST

"The village presented an animated scene. The annual return tide to the trading post was in full course and the beach was thronged with canoes and batteau laden with pelts of the winter's hunt. Voyageurs and Indians, men and women, children were here and there, a few soldiers, made up the motley crowd."—William Osler.

This was the setting on 6 June, 1822 in the isolated Michigan village of Mackinac when a shot was fired, the echo of which is still reverberating around the world. A nineteen year old French Canadian Voyageur, Alexis St. Martin was accidently shot in the abdomen. He was operated on by an army surgeon, William Beaumont (1785-1853), the only doctor in the area. St. Martin survived . . . with a permanent gastric fistula and was taken into Beaumont's home. An eye witness, Gordon S. Hubbard presented a vivid written account of the shooting:

"The late Major John H. Kinzie had charge of the American Fur Company's retail store at Michilimackinac. I was in the habit of assisting him occasionally when a press of customers needed extra clerks. The store comprised the ground floor near the foot of Fort Hill, on the corner of the street and the road leading up to the fort. The rear part of the store was underground, built of stone, which is still standing. This St. Martin was at the time one of the American Fur Company's engagees, who, with quite a number of others, was in the store. One of the party was holding a shotgun (not a musket), which was accidentally discharged, the whole charge entering St. Martin's body. The muzzle was not over three feet from him—I think not over two. The wadding entered, as well as pieces of his clothing; his shirt took fire; he fell, as we supposed, dead.

"Dr. Beaumont, the surgeon of the fort, was immediately sent for, and reached the wounded man within a very short time—probably three minutes. We had just got him on a cot and were taking off some of his clothing.

"After Dr. Beaumont had extracted part of the shot, pieces of clothing, and dressed his wound carefully, Robert Stewart and others assisting, he left him, remarking, "The man can't live thirty-six hours; I will come to see him by and by." In two or three hours he visited him again, expressing surprise at finding him doing better than he anticipated. The next day, I think, he resolved on a course of treatment, and brought down his instruments, getting out more shot and clothing, cutting off ragged ends of the wound, and made frequent visits seeming very much interested, informed Mr. Stewart in my presence that he thought he could save him.

"As soon as the man could be moved he was taken to the fort hospital, where Dr. Beaumont could give him better attention. About this time, if I am not greatly mistaken, the doctor announced that he was treating his patient with a view of experimenting on his stomach, being satisfied of his recovery. You know the result.

"I knew Dr. Beaumont very well. The experiment of introducing food into the stomach through the orifice, purposely kept open and healed with that object, was conceived by the doctor very soon after the first examination."

Beaumont was the pioneer American physiologist and probably the first United States physician to make an enduring scientific contribution. He was the spiritual descendant of Leonardo, Vesalius, Paracelsus and Paré. Beaumont followed them in daring to challenge and attempting to disprove accepted medical doctrines. He recognized his opportunity and pursued it with zeal and unselfishness rarely equalled in all the annals of Science.

Before Beaumont there were gastric fistulae and many had speculated about the digestive process. Reginald De Graaf (1664) studied artificial salivary and pancreatic juices in the dog. René de Reaumur (1683-1757), the French natural philosopher and inventor of a thermometer, Lazaro Spallanzani (1729-1799), the Italian anatomist and Johannes Müller (1801-58) the physiologist and great teacher, had suggested the chemical nature of the digestive processes. Untutored in experimentation and without laboratories or clinical facilities, Beaumont established this concept.

Beaumont was born on November 21, 1785 in the Connecticut village of Lebanon. Here he grew up and attended public school. At 21, probably prompted by the same restlessness that characterized his future life, Beaumont left his father's farm with $100.00, a cutter and horse and a barrel of cider. In the Spring of 1807 he reached the little village of Champlain, New York, near the Canadian border. Here he taught school and tended store for three years. With books borrowed from Dr. John Pomeroy of Burlington, Vermont, he read medicine in his spare time.

From 1810 to 1812 he assisted Dr. Benjamin Chandler in St. Albans, Vermont. Beaumont credits him with instilling his zeal for careful observation, logical thinking and good memory. On June 2, 1812, Beaumont was granted a license to practice by the Third Vermont Medical Society, his diploma being signed by the Dr. Pomeroy who had loaned him his first medical books.

War with Great Britain having been declared, he volunteered for service. On September 13, 1812, he arrived at Plattsburg, New York, where he was assigned as a surgeon's mate to the Sixth Infantry Regiment under the command of General James Bloomington.

Beaumont served at the Battles of York (Canada) and Sackett's Harbor. In his diary he described how the retreating British blew up the powder magazine at New York. This account of the suffering and bravery of the wounded and dying ranks with the writings of Ambrose Paré (Apology and Account of his Journeys

into Divers Places), of Stephen Crane (Red Badge of Courage), and other great war epics:

"Sail'd into harbour & came to anchor a little before the British Garrison.— We now filld the boats, & affected a landing, though not without some difficulty, & the loss of some men—the British, march'd their troops from the Garrison down the beach to cut us off in landing, & tho they had evry advantage they could not effect their design, a hot engagement ensued in which the Enemy, lost nearly a third of their min & were soon compelled to quit the field leaving their dead & wounded strewd in evry direction—We lost but very few in the engagement.—The enemy returned into garrison but from the loss sustain'd in the 1st engagement the undaunted courage of our min, & the brisk firing from our fleet, into the Garrison with 12 & 32 Ponds (pounds) they were soon obliged to evacuate it & retreat with all possible speed—driven to this alternative they devised the inhuman project of blowing up their Magazine (containing 300 Bbls Power) the explosion of which, shocking to mention, had almost totally destroyed our Army—above 300 were wounded, & about 60 killed dead on the spot by stones of all dimentions, falling like a shower of hail in the midst of our ranks—the Enemy had, about 20 killed & wounded by the expin tho the main body had retreated far out of the Garrison —After this sad disaster our Army marched into the Garrison hawl'd down the British coulours (which they were too haughty to do) & raised the American Standard on it place—Our Army was about 1500 strong— Theirs about the same—Encampt in Garrison this night —mounting a guard 500 strong to secure our safety— A most distressing scene ensues, in the Hospital— nothing but Groans, of the wounded—Agonies of the Dying are to be heard—The Surgeons, wading in blood, cutting of arms, legs & trepanning heads to rescue their fellow creatures from untimely deaths—to hear the poor creatures, crying—Oh, Dear! Oh Dear! Oh my God! my God! Do, Doctor, Doctor, Do cut of my leg! my arm! My head! to relieve me from misery! I can't live! I can't live! would have rent the heart of Steel, & shocked the insensibility of the most harden'd assassin & the cruelest savage! It awoke my liveliest sympathy, & I cut & slashed for 48 hours, without food or sleep—my God! who can think of the shocking scene, where his fellow creatures, lye mashed & mangled in every part with a Leg—an Arm—A Head, or a body ground in pieces without having his very heart pierced with the acutest sensibility, & his blood chill in his veins—then who can behold it without agonizing sympathy—"

After hostilities were ended by the Treaty of Ghent in December, 1814 Beaumont went into practice in Plattsburg. He also opened a store and advertised:

Beaumont & Wheelock have just received and offer for sale at the lowest prices a large and well-selected assortment of Groceries, consisting of Madeira, Port, London Particular, and Sherry Wines, Cognac and French Brandy, Jamaica, St. Croix and New England Gin, Molasses, Tea, Lump and Loaf Sugar, Rice, Coffee, Salt, Pepper, Allspice, Ginger, Plug and Paper, Tobacco, Pipes, Codfish, Shad, Mackerel, Chocolate, Spanish Segars, Window Glass, Snuff, Starch, Powder, Shot, Almonds, &c. Also in addition to their former stock a large assortment of Drugs & Medicines, Dye Woods, &c., &c.

— Plattsburg Republican, September 6, 1816 —

Perhaps his lack of success as a grocer was responsible for the rather sour comment in his diary:

"Trust not a man's honesty, whether Christian, Jew or Gentile.

Deal with all as though they were rogues and villains; it will never injure an honest person, and it will always protect you from being cheated by friend or foe. Selfishness or villainy, or both combined, govern the world, with a very few exceptions."

In 1819 he re-enlisted, was commissioned as post surgeon by President James Monroe and set out for Mackinac (or Michilimackinac) on his road to medical fame. Part of his trip was on the first steamboat of the west, Walk-in-the-Water. Soon after his arrival at the post, the shooting took place. In very modest terms Beaumont later reported his treatment of the wounded Alexis:

"I saw him in 20 or 30 minutes after the accident, and, on examination, found a portion of the lung, as large as a turkey's egg, protruding through the external wound, lacerated and burnt; and immediately below this another protrusion which, on further inspection, proved to be a portion of the stomach, lacerated through all its coats, and pouring out the food he had taken at breakfast, through an orifice large enough to admit my forefinger.

"In attempting to return the protruded portion of the lung, I was prevented by a sharp point of the fractured rib, over which it had caught by its membranes; but, by raising it with my finger, and clipping off the point of the rib, I was able to return it into its proper cavity; though it could not be retained there on account of the incessant efforts to cough. The projecting portion of the stomach was nearly as large as that of the lung; and it passed through the lacerated diaphragm and the external wound, mingling the food with the bloody mucus blown from the lung."

If such an accident occurred today there would be available shock therapy with nor-epinephrine, blood transfusions, oxygen, antibiotics, sedatives, well-equipped surgeries with trained assistants and good nursing care, nasogastric suction tubes, intravenous feedings and so on. It is difficult for us to grasp the skill and courage of this backwoods surgeon of 1824. His two years of devoted personal nursing care is in startling contrast to those present-day practitioners who hesitate to even place their hands on a diseased person:

". . . During this time I nursed him, fed him, clothed him, lodged him and furnished him with every comfort, and dressed his wounds daily and for the most part twice a day."

Two years after the shooting, with his fistula still open, St. Martin suddenly departed for his home in Canada. In 1829, accompanied by a wife and two children, he rejoined Beaumont at Ft. Crawford in Upper Mississippi. Beaumont kept the guide with him on a sort of retainer basis for doing light work and permitting experimentations on his stomach.

Beaumont finally realized that he would not be able to close the fistula and about three years after the accident began to write down his observations:

". . . I can pour in water with a funnel, or put in food with a spoon, and draw them out again with a syphon. I have frequently suspended flesh, raw and wasted, and other substances into the perforation to ascertain the length of time required to digest each; and at one time used a tent of raw beef, instead of lint, to stop the orifice, and found that in less than five hours it was completely digested off, as smooth and even as if it had been cut with a knife."

He was the first to study digestion and stomach movements in situ. He found that the stomach temperature was 100° F and that it fell during humid weather and rose when a dry state prevailed. He noted the effects of mechanical irritation and of various foods on digestion and gastric motility. He performed sham feeding with foods tied to a string and noted the effect of alcohol and other substances by mouth and by injection through the fistula. He disproved Magendie's view that gastric secretion was continuous.

Beaumont demonstrated that gastric juice possessed a solvent power due to some chemical constituent. The effect of gastric juice siphoned through the fistula on various foods at different temperatures was observed. He found that the digestive action decreased with lowered temperature and that cold gastric juice had no effect upon food. Among many other observations was the coagulation of milk before its digestion and the slower digestion of vegetables. He found that food removed from the stomach 20 minutes after swallowing contained sufficient gastric juice to go on to complete digestion.

Beaumont sent samples of gastric juice to Franklin Bache, Benjamin Franklin's grandson at Philadelphia and to Berzelius in Stockholm. He continued his experiments at Washington, District of Columbia (1832) and at Plattsburg Barracks, New York (1833). He described 238 experiments!

"Fistulous old Alex" was taken by Beaumont to Robley Dunglison at the University of Virginia and to Benjamin Silliman at Yale. These chemists verified that gastric juices contained hydrochloric acid and another substance, later shown to be pepsin (Theodor Schwann, 1835-1846). Claude Bernard, the great physiologist, was stimulated by Beaumont's experiments to produce gastric fistulae in various animals. By means of these fistulae Bernard confirmed Beaumont's observations and demonstrated that in the duodenum the pancreatic juice disintegrates fat into fatty acids and glycerin, starch into sugar, and proteins into amino acids.

For the rest of his life Beaumont continued his attempts to have St. Martin return for resumption of the experiments. In 1834 he was transferred to Jefferson Barracks near St. Louis. In the following year he was assigned to the St. Louis Arsenal permitting him to live in the city and to engage in private practice, a privilege formerly granted to army medical officers.

When Thomas Lawson succeeded Lovell as Surgeon General, Beaumont's army career came to an unpleasant end. Beaumont was told that Lawson was unfriendly towards him, did not realize the significance of his studies and would force him to give up his successful practice. Despite an untactful letter from Beaumont the transfer was held up for a time through the influence of friends. Finally in 1839 Lawson ordered Beaumont to Florida and Beaumont resigned. He later attempted to be reinstated by a direct appeal to President Van Buren in which he described the ability of Lawson as zero.

Beaumont attained success and distinction in St. Louis in private practice. He was said to be quick and accurate in his judgments and to inspire confidence in his patients. He was vindicated in two notable malpractice suits, in one of which he was accused of having trephined a broken skull just to see what was going on in the brain.

In his sixty-eighth year while returning from a house call, Beaumont slipped and struck his head on some ice-covered steps. He wandered about in a daze for hours. On regaining his faculties he expressed the prognosis that the injury would result in death or a paralysis. A neck carbuncle was the recorded cause of his death on 25 April 1853.

St. Martin, with his fistula, lived on until 1880. It is of passing interest that William Osler (1849-1917) unsuccessfully attempted to obtain an autopsy and to secure the famous stomach for the Army Medical Museum. St. Martin's family wired Osler, "Don't come for autopsy; will be killed." They buried the body deep in the ground and posted guards over the grave to prevent any attempted "resurrection"!

Few realize that Beaumont's studies were done before those of Claude Bernard (1813-1878) and more than a half century before the experiments of Ivan Pavlov (1849-1939). In the autumn of 1824 Beaumont sent the report of Alexis St. Martin to Surgeon-General Joseph Lovell for his corrections and approval for publication. The article appeared in the Spring of 1825 in the Medical Recorder as "A Case of Wounded Stomach" by Joseph Lovell, Surgeon-General, U.S.A. The mistake was later corrected and Beaumont was given proper credit. A more detailed account was presented in a small booklet, "Experiments and Observations on Gastric Juice and the Physiology of Digestion" (Plattsburg, N. Y., 1833). A second edition, edited by his cousin, Samuel Beaumont, was published at Burlington, Vermont (1847).

In recent years more recognition is being paid to Beaumont and his classical work. Some of America's greatest physicians have presented the Beaumont Lecture at Yale University. The U. S. Army Hospital at El Paso, Texas, has been named after him. In 1953 several papers appeared in medical journals commemorating the centenary of Beaumont's death and the Michigan State Medical Society promoted the restoration of the old American Fur Company store on Mackinac Island. The medical profession is honored by the memory of this backwoods scientist who summed up his work:

"My opinion may be doubted, denied or approved, according as they conflict or agree with the opinions of each individual who may read them; but their worth will be best determined by the foundation on which they rest—the incontrovertible facts."

Albert Fields, M.D., Los Angeles, California.

ABSTRACTS ON NUTRITION

WOODRUFF, A. W.: *The natural history of anemia associated with protein malnutrition.* Brit. Med. J., May 28, 1955, 1297.

Woodruff describes anemia in 45 pregnant natives in Nigeria. Although the anemia, always severe, might be normocytic, macrocytic or microcytic, it failed to respond to vitamin B_{12}, folic acid, or iron. It did respond slowly to increased dietary protein. Reticulocyte responses were of necessity very slow. Many of the patients had histamine-fast achylia, and the ones exhibiting macrocytic anemia all fell into this group. A very careful study of the pre-disease diets revealed lack of protein but normal calories. Enlarged liver with fatty and fibrous changes were the rule as well as splenomegaly. Malaria and intestinal parasites exerted a slightly unfavorable effect on recovery. Children with Kwashiorkor gave very similar clinical and hematological pictures. In some older children, adult males and non-pregnant females with chronic protein malnutrition and liver damage, the anemia had the same characteristics as found in young children and in pregnant women. In men a common finding was gynecomastia, and this was believed to be due to the inability of the diseased liver to metabolize estrogens. The author admits that the anemia caused by faulty protein intake is unlikely to be found outside of the tropics.

BHENDE, Y. M., VASADA, N. B. AND GANDHI, N. M.: *Edema of epidemic dropsy.* Jour. Postgrad. Med., (Bombay), 1, 1, April 1955, 27.

The authors studied 14 cases of so-called epidemic dropsy during an outbreak of the disease at Nadiad, India. It was found that hypoproteinemia is a significant factor, but there was no evidence that cardiac or renal factors played a part. Reduction of serum chloride was found to exist. The authors do not mention the possibility that the disease may have been due to ingestion of mustard oil.

RAMASARMA, G. B., SHENOY, K. G., AND PINTO, P. V. C.: *Vitamin and amino-acid content of a domestic proteolyzed liver.* J. Indian Med. Assn., 24, 15, May 1, 1955, 575.

The authors, working at the firm of Raptakos, Brett & Company, Bombay, India, have produced a proteolyzed liver preparation by combining minced liver and pancreas and autolyzing at 53° C. for 3 hours. Microbiological assay of the product was undertaken to determine its content in essential amino-acids and B-vitamins. The values obtained agree very well with those reported in the literature for proteolyzed liver made by papain digestion.

EDWARDS, W. L. J. AND LUMMUS, W. F.: *Functional hypoglycemia and the hyperventilation syndrome: a clinical study.* Ann. Int. Med., 42, 5, May 1955.

In a study of 866 consecutive ambulatory patients, 63 (7.3%) had either functional hypoglycemia or the hyperventilation syndrome. In 19 both disorders contributed to the patient's episodic symptoms. For accurate diagnosis the authors like to use voluntary hyperventilation and/or insulin administration to see if the episodes can thus be imitated or produced.

YOUNG, C. M., MOORE, N. S., BERRFSFORD, K. K. AND EINSET, B. M.: *What can be done for the obese patient? (A report of a study in an experimental clinic).* Am. Pract. & Dig. Treat., 6, 5, May 1955, 685.

The School of Nutrition, Cornell University at Ithaca, New York, undertook a survey and treatment of obese patients referred by some 39 physicians. Only about 25 percent of the patients achieved satisfactory weight reduction. No appetite-destroying drugs and no hormones were used. Persons who had become obese in childhood were most resistant to treatment. For individuals who were emotionally stable there was a high degree of success in treatment. Little or no success was achieved by those patients with deep emotional problems. The emotional condition of the individual should be defined before treatment is commenced. The only real answer to the obesity problem is prevention, aided by education of the general public. In the middle-aged, boredom should be relieved. Certain segments of the population require more physical exercise.

BERLYNE, N., LEVENE, N. AND MCGLASHAN, A.: *Megaloblastic anemia following anticonvulsants.* Brit. Med. J., May 21, 1955, 1247.

Two cases of megaloblastic anemia which developed in epileptics after the prolonged use of anticonvulsants are described. Both cases responded well to folic acid, and the evidence suggested that they were refractory to vitamin B_{12}. This anemia appears to be due to a folic acid deficiency. It is possible that phenytoin acts as a folic acid antagonist. The anemia resembled Wintrobe's anemia in hogs, one of the causative factors of which was the use of folic acid antagonists.

BODENOCH, J., CALLENDER, S. T., EVANS, J. R., TURNBULL, A. L. AND WITTS, L. J.: *Megaloblastic anemia of pregnancy and the puerperium.* Brit. Med. J., May 21, 1955, 1245.

Cases of megaloblastic anemia of pregnancy are difficult to study because treatment, which is so urgent, nullifies the signs, and, in all cases, termination of pregnancy permits spontaneous recovery. A careful study of 9 cases at the Radcliffe Infirmary, Oxford, showed that the incidence of complications of pregnancy and of the puerperium was high. No abnormality in the secretion of intrinsic factor was found in any case, nor was there any abnormality of fat absorption. The serum vitamin B_{12} levels were normal. In women treated before delivery, folic acid was more effective than vitamin B_{12}. Although an absolute deficiency of folic acid cannot be excluded, the anemia seems more likely to be due to resistance to the action of the hemopoietic factors

than to deficiency. In some cases response is noted to massive doses of vit. B_{12}.

ACHOR, R. W. P. AND SMITH, L. A.: *Nutritional deficiency syndrome with diarrhea resulting in hypopotassemia, muscle degeneration and renal insufficiency. (Report of a case with recovery).* Proc. Staff Meet. Mayo Clin., 30, 10, May 18, 1955, 207.

The case reported appears to be unique in clinical medical literature. A patient with a syndrome of prolonged nutritional deficiency that had features of pernicious anemia, sprue and pellagra, sustained an acute diarrhea resulting in depletion of body potassium. Marked renal insufficiency and acute degeneration of skeletal muscle developed and were considered to be due to the hypopotassemia. Rapid clinical improvement occurred on the use of potassium bicarbonate for a few days, plus the use of vitamins (including B_{12}) and a protein-rich diet.

BOOK REVIEWS

THE HUMAN ADRENAL GLAND. (Ciba Foundation Colloquia on Endocrinology, Vol. VIII). Little, Brown and Company, Boston, 1955. $10.00.

Edited by G. E. W. Wolstenholme and Margaret P. Cameron, the present volume describes what is known about the histological and biochemical aspects and the cortico-medullary relationships of this complicated gland, the adrenal. Additionally, there is a section on the physiological and pathological aspects and hypothalamic and pituitary relationships. Aldosterone (electrocortin) is thoroughly described. Human material was largely used, although animal experimentation also was described. While the book is of chief interest to physiologists, it has definite clinical implications, and represents a source book for physicians.

ANNOTATED BIBLIOGRAPHY OF VITAMIN E. VOL. III. National Vitamin Foundation, Inc., 15 East 58th St., New York 22, N. Y. $3.00.

The present volume of 180 pages was compiled by Philip L. Harris and Wilma Kujowski of the Research Laboratories of Distillation Products Industries of Rochester, N. Y. While it is chiefly of value to scientists and nutritionists, it is interesting reading for anyone with a medical education.

GENERAL ABSTRACTS

LASZLO, B.: *Examination of the functional state of the biliary tract and of the pancreas in viral hepatitis.* Acta Gastro-enter. Belg. 18, 2, 97, February 1955.

The author studies the state of the biliary ducts and of the pancreas during the different stages of viral hepatitis. Biliary ducts are explored by the "timed duodenal intubation" following Varela Lopez et. al. modified by Gosset and Lambling. The state of the pancreas is studied by dosage of fecal lipids, of the fermentary power of the duodenal secretions (with the ether test of Kalk-Friedrich), and of prostigmin induced serum amylase.—In the beginning of the disease, tonus is rather exaggerated; in its acme there is atony; during convalescence, hypertonic dyskinesias are again predominant. In some patients, inflammatory disease of the biliary apparatus appears, with fever, generally during the third or fourth week of convalescence. Deficiencies of the pancreatic functions (fermentary insufficiency) may take place too. The origin of the cholecysto-pancreatopathies following frequently chronic hepatitis or posthepatitis may lie—in a certain number of cases—in the functional disturbances, which take place during the acute phase of viral hepatitis. Laszlo has elaborated a pharmacodynamic proceeding to verify the results of "timed intubation." This combined method is recommended to differentiate functional spasm of the sphincter of Oddi from vaterian organic stenosis.

Franz J. Lust, M.D.

MM. R. RAYNAUD, P. MINICONI, CH. IMBERT, P. PASQUET, COUSTANT: *ICTERUS—proved on paper by Electrophoresis. (The migration of colloidial particles under the influence of an electric field in the proving of Icterus).* Arch Mal. App. Dig., 43, 12, Dec. 1954, 191.

In twelve cases of icterogenic hepatitis and in seven cases of obstructional icteric choledochus, in five cases of (gall) stone, and two cases of cancer, electrophoresis on paper has been used to bring about the selective and simultaneous fractional division of proteins, of lipoproteins and of glucoproteins of the blood serum.

A comparative study of the results obtained permit the appreciation of the relative value of the proteinogram, of the lipidogram and the glucidogram in the diagnosis and prognosis of icteri.

1. *The Proteinogram* does not present any interesting feature for the diagnosis. Hyperglobulinaemia gamma, persistent in icteri by hepatitis is also noticed in more than half of the cases of obstructional choledochus.

The rate of globulin β is normal or increased, in hepatic icteri as well as in choledochus icteri.

The increase of fractions $\alpha 1$ and $\alpha 2$, denote in the course of cancers, that one out of every two cases is positive.

The proteinogram is of no specific interest to the prognosis. The persistence of a hyperglobulinaemia

gamma, some time after the clinical cure of icterogenic hepatitis, takes away all prognostic value from this irregular group.

The Lipidogram appears to be more useful.

It is noticed that in every case of choledochus icterus the lipoproteins α are absent when tested on Black Sudan coloured bands, and in eight out of every twelve cases of icterus by hepatitis. In the four cases they are visible but very much decreased.

This disappearance of lipoproteins α, common in the two varieties of icterus, would not establish a discrimination test.

On the other hand, the rate of lipoproteins β, normal in icterogenic hepatitis, is always above normal (900mm2) in obstructional icterus.

Repeated at regular intervals, the lipidogram is permitted, furthermore, to follow the evolution and to anticipate the prognosis of icterus by hepatitis. The reappearance or progressive increase of lipoproteins α under the influence of lipotrophic medication, is an excellent sign of improvement.

The absence of lipoproteins α in the lipidogram, logical in the course of icterogenic hepatitis, since the hepatic cell is the formation spot of these lipoproteins, is less well explained when it comes from a choledochol obstruction. Perhaps the increase of lipoproteins β noticed in cases where it is not apparent, is in reality due to the adjunction of the authentic lipoproteins of Group β, of a certain quantity of lipoproteins of type α, but of abnormally slow migration.

3. *The Glucidogram,* has no value except in obstructional icterus of neoplasmic cause. In these cases, the objective, an augmentation of glucoprotein α1 and α2, is often more evident than that of the fractions similar to the proteinogram.

C. COUINAUD: *Guiding Principles in Atypical Exereses of the Liver.* Presse Medicale No. 21, 19, 3, 1955, 417.

Atypical exeresis is an ablation of a part of the hepatic parenchyma rendered imperative by lesions: hemostasis is ensured by a barrier of imbricated stitches circumscribing the parenchyma to be removed. It is actually a blind procedure which runs the risk of harming vascular or biliary elements needed by the remaining parenchyma, a fact which explains most of the deaths said to be due to "hepatic deficiency" reported after these operations. Therefore regulated exeresis is superior because of the safeguard of the hemostasis and complete respect for the vasculo-biliary elements needed for the remaining parenchyma.

However, atypical exereses have their value in certain circumstances: lesions on the edge of the liver, superficial lesions on the convex surface or on the lower surface, all those lesions whose topography and extent is such that regulated exeresis would entail too serious a sacrifice of the healthy part of the parenchyma. But they must comply with certain rules which the internal anatomy of the liver imposes. The sections must avoid the hilum region of the liver, the inferior vena cava, cutting the main right fissures which contain important supra-hepatic veins, and in the main, never make deep incursions into the parenchyma but remain parallel to the peripheral edge of the liver. Furthermore, injury to important arterial or supra-hepatic elements causes a change in the coloration of the distributing sector of these elements entailing the excision of the sector. The possible extent of these resections is studied from the topography.

Guy Albot

ARON, E. AND SABASSIER, H.: *Research on Recent Experimental Results Concerning the Vascular Pathogenesis of Gastric Ulcer.* Arch. Mal. App. Dig. 43, 12, Dec. 1954.

The authors are of the opinion that the ulcer resulting from ligature of the pylorus in the rat cannot be considered as a true experimental ulcer. The ulcer appears on a keratinized mucosa which is never in contact with the gastric secretion. Peptic auto-digestion, favored by fasting comes into play on a mucosa impaired by vasomotor reactions consecutive to ligature of the pylorus. Therefore the numerous means of prevention are not specific and this method is without interest in evaluating the efficacy of an anti-ulcerous therapeusis.

Lambling and associates have drawn attention to the role played by the kidney in the pathogenesis of this ulcer. Struck by the persistency and the importance of renal lesions, and by the absence of ulcers after bilateral nephrectomy, they thought that the kidney elaborated a vasculotrophic substance, capable of creating a lesion of the vascular system, thus rendering it sensitive to a peptic-hydrochloric attack.

Aron and Sabassier think that the external secretion of the kidney can explain this protection, as bilateral ligature of the ureters gives the same results as bilateral nephrectomy. Hyperuremia determines a lowering of the body temperature and increases the resistance of the tissues to anoxia. Experimental edema of the rat obtained by intra-peritoneal injection of ovalbumin, is not observed in uremic rats. Thus nephrectomy has an ameliorating effect on two factors determining Shay's ulcer: the cellular resistance which it increases, and the capillary permeability which it maintains.

Ulcer due to butazolidine emphasizes the part played by peptic acidity, and vascular permeability, in the pathogenic mechanism studied. Histological changes in the form of renal lesions frequently observed are concomitant with pyloric aggression and, can be observed even when there is no ulcer formation.

The authors conclude that renal participation in the ulcerous pathogenesis, by means of a pathological secretion causing lesion of the vascular system of the stomach cannot be admitted except with very great reservation.

Guy Albot

HILLEMAND, P., PATEL, J., CHERIGIE, M., NARDI, C., MENEGAUX, J. C. AND GASPAROV, A. (PARIS): *About Cancer of the Duodeno-Jejunal Angle.* La Presse Médicale 1955, 63, No. 22, pp. 445-447.

Cancers of the duodeno-jejunal angle deserve to be singled out because of their rareness (58 cases found in the literature, and 9 original cases published by one of us), because of their clinical symptoms, as well as the particular problems of surgical tactics they offer.

AMER. JOUR. DIG. DIS.

All these difficulties will be exposed rapidly with the help of four new cases.

Histologically they are of Brunnerian-Lieberkuhnian type.

Clinically two symptoms dominate: pain and vomiting.

Pains exist in 83% of the cases, frequently after meals, rarely permanent. Vomiting exists in 80% of the cases. Its frequency augments as the disease progresses. It is abundant, usually bilious, this latter being a capital character. The general health deteriorates at an early stage; anemia is frequent. A latero-umbilical tumor is sometimes found (34 out of 67 cases).

Radiological examination is important; realized with a small amount of Gelobarine and with the help of dosed compression, it allows the finding of characteristic aspects (total megaduodenum, absence of passage through the jejunum, lacunae or aspects of irregular obstruction). In cases of doubt, modifiers of intestinal contraction must be used (Atropine-Calcium, splanchnic infiltration). Evidently, even a small deformation found on several plates is suspect. But sometimes these tests can give grounds to mistakes as in our case No 1: "Man 42 years old, with pain and vomiting ameliorated by splanchnic infiltration. The patient who was lost out of sight, returned three years later with a characteristic syndrome. Operation allowed excision of a neoplastic stenosis of the angle, but post-operative slough was cause of death." In this case a pharmacodynamic test was the cause of mistaken diagnosis during three years.

Case 2 shows the difficulty of diagnosis; this was done too late: "Woman of 55, with atypical pain and vomiting; X-rays showed large growth of angle. The operation could only be exploratory, and roentgentherapy is actually leading to a slight amelioration."

Evolution is indeed inexorable in absence of surgical excision. Diagnosis is difficult as patients present various and misleading symptoms. Roentgenograms generally show a megaduodenum, which must immediately lead us to think of cancer.

The surgical tactics in use in these tumors are special, because of the proximity of the superior mesenteric pedicle, on the right, of the Treitz arch on the left, of the mesocolon above. Should one not be able to excise, a segmentary duodeno-jejunectomy should be effected. Instead of approaching the angle on the right side along the third duodenum, it seems preferable to start the liberation on the avascular left side. The tumor is then separated from the mesocolon and the small pancreas. Resection is then easy and goes quite far on the jejunum, because of the obligatory sacrifice of the first jejunal arteries, branches of the superior mesenteric. The anastomosis is duodenal-jejunal, terminoterminal or better latero-lateral. The anastomosis can be done on the left side of the mesenteric pedicle, but the excision is then more limited. It is better to effect a duodeno-vascular "uncrossing," and bring the sectioned extremities of the duodenum above the mesocolon and practice an easy latero-lateral precolic (Lahey) or transmesocolic anastomosis. Lafargue of Bordeaux has written of a case of excision following this method, and our case No. 3 is also an example of this procedure: "Woman of 55, with anemia and vomiting; a left latero-umbilical tumor is found as well as a megaduodenum on the roentgenogram. The operation (J. PATEL 22. XII. 53) consisted in excision and latero-lateral transmesocolic anastomosis. The post-operative course was simple; the patient seen in February 1955 is in an excellent state of health." If the excision is impossible a palliative operation should be attempted (gastroenterostomy or duodeno-jejunostomy) as in case 4: "Man 23 with clinical and radiological subvaterian stenosis. The operation (J. PATEL) showed an inextirpable tumor, and a duodeno-jejunostomy was done. The immediate sequels were favorable; the patient died of cachexia three months later."

Up till now results are unsatisfactory because diagnosis is often late, patients fatigued, operations difficult. Out of 67 cases one of us finds 32 excisions with 25% operative mortality, 19 patients were alive at the end of a year; 22 palliative operations with 10 post-operative deaths; the other patients were lost out of sight.

Guy Albot

CATTAN, R. AND FRUMUSAN, P.: *The Problem of the Ulcerous Disease.* La Presse Médicale, No. 20, 16, 3, 1955, p. 398-401.

In the first part of this study dedicated to the pathogenesis of the ulcerous disease, the authors consider the respective part of the hydrochloridropeptic, humoral, vascular and nervous factors.

The hydrochloridropeptic factor plays a major part in the occurrence of post-operatory peptic ulcers of the jejunum and in the production of experimental peptic ulcers of the jejunum in the animal.

Its part is more restricted in spontaneous peptic ulcus in man, where it gives only a peculiar pathological pattern to necrobiotic lesions released by other causes.

The role of the humoral factor seems less important.

The vascular factor is unquestionably very important. Its intervention has been proved on the basis of experimental, histological clinical and therapeutical data. It plays undoubtedly a major part in the mechanism of the gastric cramp seen in ulcerous patients, which in the authors' opinion is a true muscular cramp due to a transient gastric ischemia.

The influence of the nervous vegetative system is described: action of the vagus and above all the role of the irritation of the sympathetic, demonstrated by the experiments of REILLY et al.

Peptic ulcers due to spontaneous operative lesions of the brain seem also to bear evidence of this influence.

Further on, emphasis is laid on the capital role of psychism in the pathogenesis of peptic ulcer. The cortico-visceral theory of the ulcerous disease elaborated by PAVLOV's followers, especially by BYKOV et al. is presented. The advantage of this conception is the integration of the previous theories into a wider synthesis based on the predominant role of the superior nervous activity and its disorders.

In our present knowledge that theory accounts for the genuine features of the ulcerous disease, with special reference to its very special pattern of evolution. It inspired a new and interesting therapeutical method: the sleep course.

Being convinced of the capital part played by the superior nervous centers, the authors treated very severe cases of gastro-duodenal peptic ulcers by the infiltration, with novacaine, of the prefrontal brain (BUCAILLE's procedure).

The outstanding results achieved both on the ulcer and on the ulcerous bleedings are reported.

Possible deductions as to the understanding of the ulcerous disease are given, the latter being considered ultimately as the focal result of a systematic and predominantly neuro-vascular affection.

Guy Albot

MADAME PARTURIER-ALBOT, CHAMPEAU, M. AND FRILEUX, C.: *Radio-Surgery in Cases of Cancer of the Rectum.* Arch. Mal. App. Dig. Vol. 99, No. 1, Jan. 1955, p. 5.

It struck the authors that purely surgical treatment of cancer of the rectum, in spite of its outstanding success, could be improved upon.

On the one hand, Dr. M. Parturier-Albot at the Gastro-enterological Dept. of the Hôtel-Dieu, considered the extensive mutilation and the relative gravity of the operations excessive in cases of small cancers, hence the use of contact radiotherapy on small incipient cancers; on the other hand, in order to minimize the seriousness of an eventual operation, the authors have evolved a technique of associated radio-surgical treatment (assay analyzed here) for undeveloped cancers.

Dr. Parturier-Albot has proposed a new classification for cancers of the rectum:

(a) incipent or mucous cancers

(b) vegetating cancer resting on a supple or only slightly indurated base.

(c) granulating cancer resting on an indurated movable base (this type corresponds to No. 1 in the International Nomenclature)

(d) advanced cancer.

The following is an outline of the treatment:

— Contact radiotherapy alone for (a) type cancers which after an interval of up to 10 years have revealed 100% cure.

— Contact radiotherapy alone for (b) type cancers with 95% cures after intervals of up to 9 years.

— It is above all in cancers of the (c) type that the question of associated radio-surgical treatment is raised.

— For cancers of type (d), *pre-operatory contact radiotherapy* could be contemplated in some cases.

Contact radiotherapy has a twofold action:

— Locally it reduces peri-tumoral phenomena and enables particularly quiescent lesions to be operated on.

— On the general condition by clearing up diarrhea, hemorrhage and often pain, thus enabling the patient to enjoy a better general health. He can be restocked with proteins, resist anemia, increases in weight can be followed up and in this way a great proportion of operatory risks can be reduced.

The work analyzed here is limited to the study of cancer of the (c) type. Treatment begins by *contact radiotherapy.* The higher the cancer is, and in the case of low lesions, the more its situation is posterior or lateral, the better the results. The patient receives 10 to 15,000 r in contact in two treatments at weekly intervals. The results of necrosis must be judged over a period of 2 or 3 months. The speedier the development of necrosis towards sclerosis the greater the chances of a cure.

Post radiotherapic development may conform to one of three types:

1. The sclerosis softens and gives a supple scar with reconstitution of the epithelium in a padimentous form. The patient should be followed up but there is usually a *cure* in these cases.
2. Sclerosis is set up; but an *indurated* zone persists and it is impossible to tell whether there are any deep-seated neoplastic cells although superficial biopsies remain negative. In this case the authors carry out *localized exeresis* of the *rectal wall,* removing the scarred zone *simply by endo-anal operation.*

This is a delicate minor operation which is completed by an exact suture of the rectal wall which hitherto has not resulted in any complication and which only involves a 4- to 5-day hospitalization period. The removed portion is examined histologically: if a cure has been effected no more remains to be done; if there are a few neoplastic cells the usual widespread exeresis is carried out.

3. Necrosis does not develop or develops badly towards sclerosis, or *superficial biopsies remain positive.* Then the usual operation is carried out which will have the advantage of being performed on a quiescent lesion.

The authors have treated in this manner 14 cases of cancer (c):

— 1 was cured by contact radiotherapy alone

— 2 were cured by contact radiotherapy followed by a limited simple exeresis (which gave histological proof of cure)

— 3 were cured by contact radiotherapy followed by widespread but conservative exeresis (and in which examination of the portion removed showed cure of the lesion)

— 1 case remained histologically doubtful after contact radiotherapy: (after limited exeresis it was deemed advisable to perform a large scale amputation)

— 7 cases finally proved fairly conclusively to be failures as far as contact radiotherapy was concerned and were later operated on in the usual way. It should be noted that in all these cases the operation took place in better conditions and that *a ganglion was never found to be affected in the portion removed.*

Out of 14 cases, 13 were cured with a time lapse of up to 6 years (in 4 cases). The 14th case was that of a patient who had undergone contact radiotherapy alone and relapsed after 3 years: she died from an operation on a pelvic bone cavity. This patient *did not present herself for examination for 3 years as she considered herself cured.* It is here a question of a psychological failure of the method: it may prove difficult to perform

a second operation on patients who have improved considerably.

In conclusion, the authors think that, in incipient cancers of the rectum, contact radiotherapy and associated radio-surgical treatment should play an important role. It is however a method which is difficult and delicate to handle, and it should occasion no surprise that a long period of trial and error has been necessary to perfect it.

Guy Albot

AKAIWA, J.: *Studies on the furoylglycine method as a liver function test.* Kyushu Memoirs of Med. Sci., 5, 2, Sept. 1954, 141.

The injection of furoic acid (FA) into rabbits results in the urinary excretion of furoylglycine (F.G.) which gives a good color reaction. The F.G. is produced mostly in the liver (5/6th) and a small part of the kidneys (about 1/6th). The amount of F.G. formed in the liver was markedly reduced in rabbits with hepatic disease. Also the amount of F.G. produced in the kidneys was greatly reduced in rabbits with renal damage. The glycine conjugating function of the liver was markedly decreased in rabbits with acute pancreatic damage. These results confirm that the furoylglycine method may be recommended as a liver function test, even though the kidneys can partly synthesize the compound.

JENKINSON, E. L.: *The pyloric antrum of the stomach (Caldwell Lecture 1954).* Am. J. Roentgen., Rad. Ther. & Nuc. Med., 73, 6, June 1955, 905.

At some length, Jenkinson deals with abnormalities in the gastric antrum. Absence of peristalsis is an important finding in the diagnosis of organic lesions. The antrum is the most common location for both functional and organic lesions. Pyloric hypertrophy, more common in males, is believed to be a hangover from infancy, but is almost impossible to differentiate from neoplasm. Antral gastritis usually produces ulcer symptoms. Surgery seldom is required for prolapse of the gastric mucosa—a rather conmmon condition. Extragastric pathology causing deformities of the antrum is not uncommon and adds to the difficulty in diagnosis. About 75 per cent of cancers of the stomach are located in the antrum. It is better to explore and find nothing than to postpone operation in doubtful cases.

ADELMAN, B. P. AND TEPLICK, J. G.: *Intussusception of appendiceal mucoceles.* Am. J. Roentgen., Rad. Ther. and Nuc. Med., 73, 6, June 1955, 966.

Less than 100 examples of intussusception of the appendix were found in the literature since McKidd first described the condition in 1859. While appendiceal mucoceles are not uncommon, very little has been written about their x-ray aspects. The combination of these two is very rare. Only 14 instances of an appendiceal mucocele intussuscepting into the cecum could be found. The authors now add 2 new cases. From the x-ray standpoint, a barium enema disclosed a large polypoid tumor in the cecum. The terminal cecum and the appendix failed to fill. Concentric ring-like shadows of intussusception were clearly seen. Pain in the right lower quadrant, especially after meals, was a characteristic symptom. The two cases were confirmed at laparotomy and the appendix in each removed. Localized mucoceles were found in the appendix.

AYABE, M., OTA, E. AND IZAKI, S.: *Studies on cytological diagnosis of gastric cancer.* Yonago Acta Med., 1, 2, Dec. 1954, 55.

In 236 patients, 117 of whom had gastric cancer, authors used gastric lavage for collecting cytological specimens. Diagnostic accuracy by this method was 66 per cent, but in cases with clean specimens, the positive rate reaches 92 per cent. The cause of unclean specimens was pyloric stenosis and changes in the cells caused by digestion by the gastric juice. What is needed is an improvement in the method of collecting samples.

MACPHERSON, I. AND PEEL, A. A. F.: *Effects of dorso-lumbar sympathectomy on peptic ulceration.* Brit. Med. J., May 14, 1955.

The authors present the case of a 38-year-old man with severe hypertension upon whom bilateral dorsolumbar sympathectomy and splanchnicectomy was done. Following operation a duodenal ulcer, which had not been suspected of being present, progressed, producing partial pyloric stenosis. A gastroenterostomy was done but a marginal ulcer later formed and perforated, producing peritonitis. Eventually a 4/5 gastric resection was done. Five years later the patient's blood pressure had returned to its original high level (230/130). Upper abdominal visceral sensation which had been destroyed by the spinal operation masked the symptoms of the peptic ulcers, although pain was present when peritonitis occurred, because the afferent fibres from the peritoneum do not travel with the sympathetic nerves. Obviously, peptic ulcer should be looked for prior to sympathectomy.

ROWLANDS, B. C. AND KING, P. A.: *Immediate partial gastrectomy for perforated peptic ulcer.* Brit. Med. J., May 21, 1955, 1254.

The operation of partial gastrectomy was done in selected cases of perforated peptic ulcer. The criteria for selecting patients for the operation included (a) any perforated gastric lesion, (b) large perforations, (c) a history of previous perforation, (d) a long history of ulcer dyspepsia and (e) concurrent hematemesis. Fifteen cases were selected for immediate gastrectomy in a series of 54 perforations encountered in a period of 30 months. There were two fatalities. In the others, recovery was uneventful.

MAINGOT, R.: *Congenital atresia of the bile ducts: report of a case successfully treated by cholecystojejunostomy.* Brit. Med. J., May 21, 1955, 1256.

Jaundice in a newborn child calls for exploratory operation as soon as a diagnosis of obstructive jaundice has been completed. A search must then be made for any evidence of extrahepatic biliary passages which might be used to establish a free flow of bile into the intestinal tract. Fully 20 per cent of cases of atresia of the bile ducts can be cured by choledochoenterostomy or cholecystoenterostomy. The author describes the technique of these operations. A case is presented of congenital

atresia of the common bile duct which was successfully treated by cholecystojejunostomy combined with enteroanastomosis.

LOREMIR, A. AND ROTHBERG, M.: *Polyps of the esophagus.* J. Indiana State Med. Assn., 48, 5, May 1955, 493.

An interesting case is presented of a farmer who suffered from dysphagia for 7 or 8 years. One morning he suddenly regurgitated a fleshy mass into his mouth, an incident accompanied by marked dyspnea. The family physician was called and cut the mass off after ligation at its narrow pedicle. The specimen was gourd-shaped, the neck portion was 4 cm. long and 1 cm. wide, while the body was 5 x 3 x 2.5 cms. On section the tissues appeared to be of fat covered by a thin gray layer. Centrally there were longitudinally coursing blood vessels. No evidence of malignancy was found. The patient refused further investigation and is well.

BENNETT-JONES, M. J. AND O'DOMHNAILL, S.: *Vagotomy with gastro-enterostomy for duodenal ulcer.* Brit. Med. J., May 14, 1955, 1183.

The authors regard vagotomy combined with gastrojejunostomy as at least the best second-choice operation for duodenal ulcer. Excluding cases of acute bleeding, but including a few cases with perforation which required more than simple closure, the operation of abdominal vagotomy combined with a low gastro-jejunostomy is a very safe procedure and produces good results in 88 percent of cases, for at least 4 to 6 years. When the operation failed to relieve the symptoms, Billroth I conversion was the most satisfactory secondary procedure. Vagotomy combined with a Billroth I partial gastrectomy may indeed prove to be the best primary procedure. Vagotomy should be included in the treatment of duodenal ulcer because only 50 percent of permanent good results can be expected from gastroenterostomy alone.

J. A. M. A. 158. May 7, 1955, pp. 44-45. *Council on Pharmacy and Chemistry: Candy medication and accidental poisoning.*

While medicine put up in candy form for children increases the acceptability of the drugs by disguising taste and flavor, there is increasing evidence of poisoning by such products. This applies particularly to aspirin in candy form. This type of product now is sold over-the-counter in drug stores and constitutes as much as 12 per cent of the total aspirin sales. 80 per cent of aspirin deaths have occurred in children under 5 years of age. Several suggestions are offered to lower the risk of poisoning from this and similar products.

BOGSCH, A.: *Contribution to the question of the stabilization of functional diverticula of the esophagus. (Beitrag zur Frage der funktionellen Speiserohrendivertikel).* Fortsch. Roentgen. 82. 5. May 1955.

Long standing diverticula of the esophagus can become stabilized. The radiological picture of the esophagus in these cases is very characteristic. It can imitate the colonic haustration with normally broad sections alternating with circular dilatations. Differentiation from other smooth-walled esophageal dilatations is not difficult.

Franz J. Lust

GIMES, BELA: *"Phantom pains" after stomach resection. Der "Phantomschmerz" der Magenresezierten.* Fortschr. Roentgen. 82, 5. May. 1955.

Four hundred patients with different complaints who underwent a gastric resection because of ulcer were examined. In 62 cases the patients had exactly localized pains on the right side of the resected stomach stump corresponding to the spot where the ulceration had been localized in the resected part. Radiologically demonstrable changes which might explain these pains were not found. To explain this sort of pain we must suppose a mechanism similar to that of the phantom pains of amputated extremities. The phantom pain of the patients with gastric resection must be regarded as a pain, which appears after the plexus pyloricus has been severed and arises by projection into the preoperative area.

Franz J. Lust

NIEMETZ, D. AND WHARTON, G. K.: *Benign gastric polyps.* Ann. Int. Med., 42, 2, Feb. 1955, 339.

Thirty-two cases of benign gastric polyps have been studied. Gastroscopy was found superior to x-ray in the diagnosis of polyps, but the use of both procedures affords the best results. The symptoms of gastric polyps are protean and none is pathognomonic, but abdominal discomfort, nausea and vomiting, and loss of weight are common. In no case did the authors encounter malignant degeneration of benign gastric polyp.

CAWKWELL, W. I.: *Acute perforation with peritonitis as a complication of carcinoma of the colon.* New Zealand Med. J., 54, 300, Apr. 1955, 187.

Cawkwell describes the case of a man of 34 with an adenocarcinoma of the sigmoid whose first symptoms were pain from perforation of the cancer and peritonitis. Following excision he had 5 years of good health. Then the tumor recurred and 16 cms. of the colon were removed. Four months later he developed fever and a mass in the left iliac fossa. Antibiotics and colostomy, however, failed to save his life and he died from acute toxemia 2 days later. The incidence of acute perforation complicating cancer of the colon is between 3 and 5 per cent of all cases. The condition carries a poor, but not necessarily hopeless, prognosis.

BLACK AND BLUE

Bloomington, Ind.,—Bruises and black-and-blue marks, once the season-long badge of the athlete engaged in football, soccer, lacrosse, boxing and other "contact" sports, can be sharply reduced in both incidence and duration with the use of modern medicines, a New York doctor declared here today.

Dr. A. Lee Lichtman of Manhattan's Polyclinic Hospital told delegates to the National Athletic Trainers' Association annual conference at Indiana University that bruises can be reduced in severity if the athlete is conditioned in advance with vitamins, and if injections of the enzyme trypsin are given immediately after an accident to quickly reverse the inflammation and swelling that tend to occur.

"Under this regimen, we see bruises that would ordinarily be painful for ten days subside almost overnight," the doctor said. He cited three days instead of two weeks as the recovery time for unusually bad bruises.

Dr. Lichtman based his remarks on experience with athletes who appear in Madison Square Garden, just across the street from Polyclinic hospital. In the past few years he has treated boxers, basketball players, rodeo bronc busters, and circus acrobats, among others subject to traumatic injury.

To condition athletes before their encounters, Dr. Lichtman gives them hesperidin—a substance found in citrus fruits, especially in the meaty parts—and ascorbic acid (Vitamin C). When used together, these citrus fruit derivatives strengthen the smallest blood vessels of the body, the capillaries. A bruise is chiefly a mass of damaged capillaries which allow blood to leak into surrounding tissues, said the doctor.

Although capillaries will break under a heavy blow even if they're functioning well, Dr. Lichtman reasons that healthy capillaries will resist breakage to a greater degree than fragile ones.

Once a bruise-causing blow has been struck, Dr. Lichtman gives an injection of the purified enzyme trypsin in the buttock as soon as permitted by the rules of the game. In a manner yet unexplained, the trypsin rapidly moves to the affected area to reverse the inflammatory process, he said.

In prize fighters, black eyes and other bruises have subsided in one to three days, instead of the normal ten days to two weeks, the doctor reported. However, the treatment has little effect on the black-and-blue color once it sets in, he said, emphasizing the importance of giving the injection before discoloration starts.

In all, Dr. Lichtman said he had used the vitamin and enzyme treatments on 124 athletes who had suffered bruise-causing blows. He classed the results as excellent in 85 cases, and good in 36. In the remaining three, there was no response; in all three the blows had ruptured veins, posing a different therapeutic problem, he said.

Dr. Lichtman told his audience of collegiate sports trainers that athletes present problems far from the ordinary practice of medicine. Where the average person seeks a doctor when he is sick, and is satisfied with a gradual return to health, the athlete aims for top physical condition before his effort, and wants not only a perfect recovery from injury, but wants it as quickly as possible.

"As pointed out earlier this month by Dr. Joseph D. Wolffe, president of the American College of Sports Medicine, too much of our medical knowledge is based on study of sick people, and not enough about those in good health," Dr. Lichtman said.

"Athletes are by no means the supercreatures many people imagine them to be," said the doctor. "They are usually good athletes because they have good timing, excellent reflexes, and coordination, but may at the same time be suffering from ills. Such ailments, often affecting only the top ten percent of body efficiency, would be unnoticed by most people, but in the athlete they interfere with his best performance."

Dr. Lichtman outlined treatments that have tried over the years to bring athletes into top condition just before an event. Diet, training and practice can do only so much along this line, and there has been a long search for medical aids, he said.

A substance called glycine, found in gelatin, was tested some years ago, and found to produce some increase in efficiency, but not enough to be significant.

Similarly, the male hormone testosterone was found valuable as a pre-game "supercharger," but had the undesirable side effect of upsetting the body's delicate hormone balance.

Better supply of oxygen to the muscles, either by breathing oxygen-enriched air or by better utilization of the oxygen in ordinary air, is the key factor in obtaining better performances over a sustained period, according to Dr. Lichtman.

Experiments in which a distance runner ran on a treadmill, with oxygen-enriched air supplied from a tank alongside, showed that top speed can be maintained twice as long as with ordinary air, he said.

Noting that all athletes do not have the huge lungs of champion swimmers or of England's Dr. Bannister who first broke the four-minute mile, Dr. Lichtman said he had been experimenting with various substances in an effort to find one that would help an athlete get better use of the oxygen in ordinary air. Preliminary experiments with massive doses of Vitamin B-12 provide hopeful results, he said.

"Although these things are extremely difficult to assess, boxers and runners heavily fortified with B-12 seem to perform much better than without it," he reported. Experimentally, daily shots of 1,000 micrograms of B-12 were given for six days before the event.

Since physiologists generally agree that Vitamin B-12 cannot be stored by the body in excess of normal requirements, it appears that the "extra energy" effect is a function in addition to its role as a vitamin, the doctor said.

"I am not at all satisfied with explanations so far advanced for this phenomenon, but I can't argue with the results I see in athletes," he added.

On the question of whether such medicinal "superchargers" amounted to unfair tactics, Dr. Lichtman said he had often wondered what attitude sports officials might take. It would be hard for anyone to criticize measures taken to strengthen capillaries physiologically, or to treat a bruise when a blow is struck, he feels.

The massive doses of B-12 may be another story, but they can hardly be classed with narcotics, in the doctor's opinion.

"As a physiologist and surgeon, I am not concerned with who wins, but only how well my patient sur-

vives the stress of the game," he said.

For trainers of college squads, the doctor made no recommendation for large doses of B-12, since his findings in that field are still regarded as experimental. But he did advise that squads in practice take capsules called Hesper-C (hesperidin and Vitamin C) three times a day during the season, and that attending doctors have trypsin ready for intramuscular injection when a traumatic injury occurs.

"And a little bit of B-12—say a 25 microgram tablet three times a day—can do no harm, and will insure that any slight deficiency of oxygen - carrying hemoglobin is brought up to normal," he said.

GOOD NEWS FOR DIABETICS

A new cookbook, THE DIABETIC'S COOKBOOK, will be published this fall. It contains 250 recipes for preparing beverages, pastries, desserts, fruits, meats, salads, sandwiches, and vegetables. American Diabetic Association values and exchange lists are used throughout the book. Also, pages are included for the diabetic to fill in his own diet prescription. Every recipe shows total amounts of carbohydrates, proteins, and fats as well as the caloric value of each serving. Therefore, with this information plus the diet prescription, all in one book, the diabetic can readily prepare 250 delicious and tested dishes that fit in his diet.

Indeed, THE DIABETIC'S COOKBOOK is such a practical cookbook for diabetics that Dr. Charles H. Best, one of the discoverers of insulin, has written the introduction. In it, he says, "I have no hesitation in recommending this book most highly and I feel sure that a very large number of diabetics—and their families—will welcome its publication and will profit by reading it."

The author of THE DIABETIC'S COOKBOOK, Mrs. Clarice B. Strachan, of Tulsa, Oklahoma, developed and proved the recipes over a period of 14 years during which she cooked for her diabetic son. Mrs. Strachan has combined a strong scientific background with the delicate artistry of the kitchen to produce a volume which will add variety and zest to the diabetic's menu.

THE DIABETIC'S COOKBOOK is published by The Medical Arts Publishing Foundation, 1603 Oakdale Street, Houston 4, Texas. The price is $6.50. Copies can be obtained from your bookstore or by writing directly to the publisher.

NEW MALARIA DRUG ACTS FAST AGAINST VIVAX AND FALCIPARUM

La Lima, Honduras—Plaquenil, a new antimalarial compound, resulted in rapid clinical improvement in 213 cases of P. vivax and P. falciparum infections, without any toxic effects, according to Dr. Mark T. Hoekenga of the United Fruit Co. Hospital here.

Writing in the American Journal of Tropical Medicine and Hygiene (4:22, 1955), he says the new antimalarial was given orally and parenterally to Honduran natives ranging in age from seven to 65 years. Developed at the Sterling-Winthrop Research Institute, Plaquenil is presently under clinical study by Winthrop-Stearns Inc.

Dr. Hoekenga reports that parasites disappeared and fevers were brought down to normal in 18 to 48 hours. These results were obtained both in an orally treated group of 150 patients and in the 63 who received Plaquenil intramuscularly or intravenously. Single doses of varying concentrations were used for all 213 cases. Treatment failed in eight cases and only three relapses were noted. The latter were retreated and had no further relapses at the end of one year's observation.

As confirmed by frequent clinical and laboratory tests, no toxic effects were found in any of the treatment regimes. There were no local reactions to gluteal injections among the group given intramuscular injections; nor any appreciable change in pulse or arterial blood pressure in the series treated by vein.

ASPIRIN AND DEMEROL SUGGESTED IN CHILD'S RECURRENT HEADACHE

Rochester, Minn.—Children complaining of recurring headaches as their only symptomatic disorder get effective pain relief from aspirin alone or in combination with another analgesic like Demerol or codeine, Dr. Haddow M. Keith of the Mayo Clinic states in *Pediatric Clinics of North America* (May 1955).

Without pain relief, such children are often easily upset, irritable and fatigue rapidly, he notes, adding that it is usually difficult to diagnose the causes and eliminate them. Studying 100 children between the ages of two and 15, Dr. Keith reports that 43 probably had migraine headaches. The etiology in 30 cases was unknown. Other causes were: infection with fever, ocular abnormalities, persistent sinusitis, fatigue, psychogenic, allergic, and post-traumatic factors.

The underlying cause of the headache symptom must be determined, if possible, before intelligent treatment can be prescribed. Then, if the headache is due to such causes as acute infection, brain tumor or nephritis, therapy can be started immediately and is generally helpful, he says.

Aspirin is recommended by the author as symptomatic treatment, especially "when the more specific treatment requires time to exert its beneficial effect." Suggested aspirin dose is one grain per year of age up to five years. In some cases, aspirin may be combined with Demerol or codeine.

The study showed ergotamine in combination with caffeine to be effective in most cases of migraine in children. Dr. Keith says that aspirin was effective in one-quarter of the cases of migraine treated.

ALEVAIRE EFFECTIVE IN 84% OF "PREMATURES" RESPIRATORY ILLS

New York—The mucolytic detergent Alevaire "is a most useful adjunct" in the treatment of respiratory tract diseases particularly in premature infants, as well as adults and children, a group of investigators at St. Vincent's Hospital here state. Their report appears in the *New York State Journal of Medicine* (55:1587, 1955).

The effectiveness of the drug, manufactured by Winthrop-Stearns Inc., in facilitating elimination of secretions was evaluated in a series of 300 patients representing pediatric, medical and surgical problems. The series included 181 adults, 62

babies up to the age of four, and 57 prematures. Most adults had chronic respiratory diseases while a majority of the infants and children had acute conditions, according to Andre Smessaert, M. D., V. J. Collins, M. D., and V. D. Kracum.

They found "the highest incidence of good response occurs in conditions affecting infants and children." In the premature group 72 per cent of the cases treated had a good response and an additional 12 per cent had a significant response "for a total of 84 per cent showing marked improvement accompanying the use of Alevaire."

Of the 300 patients, aerosol inhalation of Alevaire provided "significant benefit to 70 per cent." Poor responses were noted in only 15 per cent.

The therapy is "harmless to the patients, has no contraindications and can be used for prolonged periods of time," the authors state. One of the chief advantages of Alevaire cited is that "unlike many other detergents it is not hydrolyzed by tissue enzymes and thus retains its surface-active properties for a long time after administration." No untoward reactions were observed in patients receiving Alevaire for as long as six weeks.

Most gratifying results were obtained in newborn infants, premature or at term. Referring to results in neonatal atelectasis as "impressive," the doctors say, "this dreaded condition is usually improved in a few hours.

"It was really striking to see a cyanotic baby with gasping respirations and suprasternal retraction become relaxed and pink in such a short period of time."

Other acute conditions in which Alevaire was found useful were: Laryngitis, bronchitis, bronchiolitis, pneumonia and asthma. Antibiotics and sulfa drugs were also employed in most cases, but "it was the general impression that surface agents constituted a most valuable adjuvant and made recovery easier and faster in the treatment of the croup and edema of the vocal chords.

"Alevaire has been more satisfactory and more effective than plain humidification," the report says.

The drug also proved useful in chronic respiratory diseases in adults where "abundant and often viscid secretions create a serious problem." Improvement may take 48 to 96 hours, but "patience and perseverance are rewarded," the New York investigators write.

NEW BRONCHODILATOR REPORTED ORALLY EFFECTIVE AND SAFE

An unusual new bronchodilator drug that may provide an oral, safe means of preventing attacks of asthma as well as relieving them was reported at the annual meeting of the National Tuberculosis Association and the American Trudeau Society in Milwaukee.

Dr. Hollis G. Boren of Houston said the drug was effective orally in improving ventilation in various respiratory conditions and was apparently free from significant side effects even after prolonged maintenance dosage. Palpitation and tachycardia are effects often associated with the use of other bronchodilators, many of which are sprayed or injected.

"Striking improvement" was demonstrated in some cases even though the patients had previously failed to respond to a full therapeutic program, Dr. Boren said.

Dr. Boren is the first physician to to report on clinical tests of the new bronchodilator, synthesized by Lakeside Laboratories, Inc. and known as JB-251. Clinical research is under way in many other institutions, and other reports to the profession are expected.

JB-251 is N-(2-(3,4 methylenedioxyphenylisopropyl) norepinephrine hydrochloride. The JB stands for Dr. John Biel, chief of the medicinal chemistry division at Lakeside.

Dr. Boren strongly emphasized the importance of employing mechanical technics to measure the action of drugs on the respiratory function. He determined the resistance to airflow, crucial in bronchial asthma, by simultaneous measurement of intra-esophageal pressure and associated lung volume and flow changes. Complete mechanical studies of breathing were done in 36 cases to evaluate the drugs. The studies indicated the frequency with which the pressure fluctuations were decreased and the increased volume of air ventilated following use of JB-251 and others in the Lakeside series.

Dr. Boren is assistant chief of the tuberculosis service at the Veterans Administration Hospital, Houston, Texas, and instructor in medicine at Baylor University School of Medicine. He was assisted by Dr. Carroll A. Handley, professor of pharmacology, and Demitri J. George, medical student.

RELIEF IN ASTHMA CASES OBTAINED WITH ALEVAIRE

Sun Valley, Calif.—Effective relief has been obtained in a large percentage of cases of acute and chronic asthma with aerosol inhalations of Alevaire, a mucolytic detergent, according to Dr. D. Edward Frank here.

Writing in *Annals of Allergy* (13:313, May-June 1955), he says a study of ten patients during acute asthmatic attacks revealed that five reported from 50 to 100 per cent relief following Alevaire inhalations. Two of the ten cases obtained 100 per cent relief despite such complications as emphysema and bronchiectasis. Alevaire is manufactured by Winthrop-Stearns Inc.

Results were even more encouraging when Alevaire was used to treat 14 patients with chronic asthma. All patients received at least 50 per cent symptomatic relief, with 11 of the 14 reporting 80 per cent relief. Half of the latter group, Dr. Frank states, stopped using all symptomatic medication.

The course of therapy consisted of inhaling nebulized Alevaire for 15 minutes, one to three times weekly for periods ranging from one to four months. Purpose of the procedure was to liquefy tenacious mucous plugs obstructing the bronchial tree, and to eliminate the exudate by coughing. Referring to the drug's effectiveness in this respect, Dr. Frank observes:

"One cannot help but feel that the more prolonged each treatment, and the more frequent the treatments, the greater the potentialities for reducing viscid exudates or plugs in bronchi into thin, easily evacuated secretions."

STERANE, NEW ANTI-ARTHRITIC & ANTI-INFLAMMATORY STEROID, MARKETED BY PFIZER LABORATORIES

New York, N. Y. July 8—Sterane, a powerful anti-arthritic and anti-inflammatory steroid four to five

times more potent than cortisone or hydrocortisone, was placed on the market today by Pfizer Laboratories, according to an anouncement by Thomas J. Winn, vice-president of the company.

Sterane (prednisolone) is a crystalline steroid, related to, but chemically different from hydrocortisone. It is being mass produced economically by Pfizer through a unique combined chemical synthesis and fermentation process.

The new steroid is similar to cortisone and hydrocortisone but offers the advantages of being quantitatively superior and relatively free of serious, permanent side effects, according to Mr. Winn.

Sterane is indicated in the treatment of rheumatoid arthritis and other conditions, including bronchial asthma, ulcerative colitis, lupus erythematosus, pemphigus, scleroderma and other allied collagen diseases.

It has not proved effective as a topical anti-inflammatory agent, Mr. Winn stressed.

Electrolyte studies of serum and urine of patients receiving Sterane have revealed an absence of significant sodium retention or potassium depletion.

Conservatively figured, he said, sales of Sterane and similar products will probably account for an industry-wide annual total of $25-million. This is considerably more than half the estimated $35 to $40-million annual business now done by all corticoid products.

The Sterane tablet (5 mg.), oval-shaped, scored, and Pfizer imprinted, not only is distinctive but has been designed for ease of administration by the arthritic patient, according to Mr. Winn.

In clinical studies, the initial suppressive dose for rheumatoid arthritis averaged 30 mg. daily and the maintenance dose ranged from 5 mg. to 20 mg. Comparative hydrocortisone maintenance doses usually range from 30 mg. to 50 mg.

"Sterane is a powerful new weapon in the fight against the great crippler, arthritis," Mr. Winn said. "Because of its potency and relative freedom from undesirable side effects, it may well replace cortisone and hydrocortisone in the treatment of rheumatoid arthritis. Sterane, he said, will thus prove a potential aid for some 200,000 persons now regarded as permanently disabled and "of great help to some 10,000,000 others who suffer from rheumatoid diseases in one degree or other."

PFIZER PRESCRIPTION SPECIALTY: STERANE

WHAT THE PRODUCT IS: A synthetic crystalline steroid hormone. Sterane (prednisolone) is an analog of hydrocortisone.

WHAT IT'S FOR: Treatment of rheumatic arthritis and such conditions as bronchial asthma, pemphigus vulgaris, acute disseminated lupus erythematosus, exfoliative dermatitis, atopic dermatitis, ulcerative colitis, periarteritis nodosa, scleroderma and dermatomyositis.

ADVANTAGES: In clinical trials, Sterane has proved to be four to five times more potent than cortisone or hydrocortisone as an anti-rheumatic or anti-inflammatory agent. It is similar to cortisone or hydrocortisone in suppressing rheumatoid arthritis, but is quantitatively superior and relatively free of significant metabolic, water or electrolyte disturbances.

HOW ADMINISTERED: Orally. Suppressive dose for rheumatoid arthritis averages 30 mg. daily. Maintenance dose ranges from 5 mg. to 20 mg. (Cortisone maintenance doses usually range from 30 to 50 mg. daily.)

HOW IT'S SOLD: In bottles of 20 tablets, each containing 5 mg. of Sterane. Tablets are oval-shaped, scored and distinctively imprinted with Pfizer name.

WHO MAKES IT: Pfizer Laboratories, division of Chas. Pfizer & Co., Inc., N. Y.

JAMES G. WILSON

Gainesville, Florida, July — Dr. James G. Wilson, professor of anatomy at the University of Cincinnati, has been appointed to head the anatomy department of the University of Florida's College of Medicine, Dr. J. Wayne Reitz, University President, has announced following Board of Control approval.

Dr. Wilson's appointment became effective September 1 of this year. The University's College of Medicine plans to admit its first students in September, 1956.

Dr. Wilson was born in Clarksdale, Miss., April 2, 1915. He received a BA degree in biology and chemistry from Mississippi College in 1936, an MA degree from the University of Richmond in 1938, and a PhD degree in anatomy and endocrinology from Yale University in 1942. He also attended Brown University for one year.

Prior to joining the faculty of the University of Cincinnati as associate professor of anatomy in 1950, Dr. Wilson was a member of the anatomy department at the University of Rochester for eight years, where he served as section head of Embryology of the University's Atomic Energy Project in 1947-1950. He was consultant on embryology on the project during 1950-53.

He has been professor of anatomy at the University of Cincinnati since 1954, where he is in charge of the course on gross anatomy. He is a member of the Faculty Council of the Medical College, which has advisory powers to the dean, and is faculty advisor to the Student Council of the Medical College.

Dr. Wilson is a member of Sigma Xi honorary scientific fraternity, the American Association of Anatomists, Rochester Academy of Science, The Society of Experimental Biology and Medicine, and the Society of Human Genetics. He has had numerous publications in leading scientific journals.

He is married and has three children.

PARKE, DAVIS & COMPANY ANNOUNCES NEW COMBINATION OF TWO ANTIBIOTICS TO BATTLE INFECTIONS

Detroit, — Parke, Davis & Company has announced a new antibiotic preparation, combining two drugs, Chloromycetin and dihydrostreptomycin, for the treatment of various enteritic infections.

Called Chlorostrep, the new preparation has been successful in treating susceptible infections of the diarrheal type, and mixed infections encountered in bowel surgery.

Chlorostrep is the 12th form of the Parke-Davis antibiotic Chloromycetin to be introduced to the medical profession since it was developed from the mold found in a specimen of soil from Venezuela.

Wide laboratory and clinical testing has proved that Chlorostrep is

more effective in many instances than is either drug alone, the company said.

A team of two medical investigators reported on the use of Chlorostrep in a 39-year-old patient with pulmonary tuberculosis, active sacroiliac and sacral tuberculosis and a tuberculous rectal fistula. Therapy was instituted on a dosage schedule providing 250 mg. of each antibiotic every six hours. The rectal fistula closed completely without drainage after 27 hospital days, although chemotherapy was continued for a total of eight weeks after admission. The antibiotic combination was employed also in patients with chronic anal fistula of the horseshoe variety, in which healing appeared to be definitely facilitated.

The antibiotic combination has been used both preoperatively and postoperatively in patients with infected pilonidal cysts with draining sinuses. Healing was observed to be almost by primary intention.

"In two instances, healing of chronic draining sinuses occurred following Chlorostrep therapy subsequent to burning out of granulation tissue in the sinus tract," the company said.

Chlorostrep Kapseals, available only on physician's prescription, each contain 125 mg. Chloromycetin (chloramphenicol, Parke-Davis) and 125 mg. dihydrostreptomycin (as the sulfate). They are supplied in bottles of 12 Kapseals.

The suggested dosage of Chlorostrep in dysenteric enteritis is 1 to 4 Kapseals every 6 hours. Preoperatively, Chlorostrep should be given in dosage of 1 to 4 Kapseals every 6 hours during three or four days before surgery and, when fluids are resumed, for five to six days after. In tuberculous patients, daily total dosage of Chlorostrep should be increased, or the usual dosage given over a longer period.

ANGIOGRAPHY WITH DIODRAST CALLED VALUABLE DIAGNOSTIC AID

Winnipeg, Man.—Cerebral angiography performed with the contrast medium Diodrast proved to be an "extremely valuable" diagnostic procedure associated with comparatively little risk, Drs. Dwight Parkinson and A. E. Childe state in the *Canadian Medical Association Journal* (72:571, 1955).

They report on 266 angiograms obtained in a series of 200 patients at Winnipeg General Hospital. Although the overall diagnostic value of angiography does not equal that of pneumography, the former method should be used more frequently as a primary procedure in cases of suspected brain tumor. The doctors note significantly, however, that none of the patients with normal angiograms were later shown by pneumography to have brain tumors. It is also suggested as a routine in certain cases of suspected vascular anomalies, the authors say.

Approximately 90 per cent of the 266 angiograms were excellent or satisfactory from a diagnostic standpoint. Ten per cent were failures "due more frequently to the surgeon's technique or the patient's movement than to mechanical failure." A 35 per cent Diodrast solution was administered percutaneously, each patient receiving three injections. Four films at one-second intervals were taken after each injection.

Diodrast is manufactured by Winthrop-Stearns Inc.

PFIZER RESEARCHERS DEVELOP DEFINITIVE ANALYTICAL METHOD FOR ASSAYING RESERPINE

Researchers of Chas. Pfizer & Co., Inc., have successfully developed definitive analytical methods for the assay of reserpine in its pure as well as crude and prepared dosage forms.

An alkaloid found in species of the tropical and semi-tropical rauwolfia plant, Reserpine has been finding wide use in the treatment of mental diseases and hypertension.

Using especially devised techniques, the researchers — H. W. McMullen, H. J. Pazdera, S. R. Missan, L. L. Ciaccio and T. C. Grenfell — were able to determine the identity, purity and percentage amount of the pure chemical reserpine compound in hundreds of samples of the drug and a wide variety of the rauwolfia plants.

A paper written by the five-man team and appearing currently in the July issue of the *Journal of the American Pharmaceutical Association*, Scientific section, describes the methods employed for determining the physical constants of reserpine. In describing the methods used the authors said that these analytical methods "have shown to be applicable to the analysis of the pure compound, crude root extracts and pharmaceutical preparations."

Three tests, all conclusive in their aims and results, were utilized: ultra violet absorption, paper chromatography and fluorescence. It was pointed out that not one test, but rather a correlation of the three was used, thus affording specific proof "beyond coincidence."

"By establishing the chemical and physical properties of reserpine through these scientifically worked-out methods," they point out, "such cost-consuming factors as labor and time necessary for developing analytical techniques are eliminated for all pharmaceutical manufacturers."

The authors explained that roots of the different rauwolfia species vary considerably in content and in composition of alkaloids.

"Since," they write, "the alkaloids are used in pharmaceutical preparations as pure compounds, as crude extracts and as whole ground root, it is necessary to establish the properties of these alkaloids, methods of identifying them in the presence of similar compounds and methods of determining the quantities present in pharmaceuticals.

Chas. Pfizer & Co., Inc., manufacturers of antibiotics, hormones, vitamins and fine chemicals, extracts and produces crystalline reserpine and offers both the crystalline material and a 1% trituration in commercial quantities.

MYSURAN CALLED MORE EFFECTIVE THAN NEOSTIGMINE IN MYASTHENIA GRAVIS

Boston—Mysuran, a new compound under clinical study, has "approximately twice the duration of action of neostigmine" in treating myasthenia gravis and produces fewer side effects, according to tests conducted by Dr. Robert S. Schwab and colleagues at Massachusetts General Hospital.

The report on Mysuran, which was developed by the Sterling-Winthrop Research Institute, appears in the *Journal of the American Medical Association* (p. 625, June 25,

1955). In a study of 50 patients, the investigators say 41 obtained greater benefits from the drug than from all previous medication. A footnote states that the number of patients treated with Mysuran was subsequently increased to 75, of whom "59 are still taking the drug."

Therapy with the new preparation was first started in 30 female and 20 male cases of myasthenia gravis. Seventeen of the 41 patients who have continued using Mysuran in place of neostigmine or other compounds experienced a significant reduction in side reactions, and "another 20 reported a very definite prolongation of the effect." In no case did a patient take more Mysuran than neostigmine. There were no side effects of the anticholinesterase type and urinalyses, blood studies and physical examinations revealed no involvement of other organs, the investigators note.

Discussing parenteral therapy, the authors found "intravenous doses as small as 125 mcg. produced a definite antimyasthenic response" in ten minutes, lasting between two to three hours. The good response was maintained, without reactions, when the dose was cautiously raised by degrees to 250 mcg. Intramuscular injections produced nearly the same effect after a longer interval of 20 minutes. "Minimal" gastrointestinal disturbances occurred after parenteral use, it is reported. Mysuran was also administered as a syrup for oral use during the clinical tests, and proved life-saving in a case where other drugs were unavailing.

EXAMINATION OF COLON AND RECTUM

Routine examination of the colon and rectum as a part of every complete physical examination of every adult patient in order to find tumors before symptoms develop and malignant degeneration occurs is recommended by Dr. Neil W. Swinton in the Lahey Clinic number of *Surgical Clinics of North America*, (35:833 (June) 1955).

Technical improvements in enema preparations, which are now available in disposable polyethylene containers, have facilitated the preparation of patients for sigmoidoscopy, writes Dr. Swinton.

"These have made it possible for us to give cleansing enemas satisfactorily with a minimum of time and equipment," he says. "We have used these disposable units for several thousand patients and we have found them as effective, or more so, than soapsuds enemas." The preparation of patients who give themselves an enema at home is described as unsatisfactory.

Polyps are found in approximately 5 per cent of patients, regardless of symptomatology, who are examined by sigmoidoscope at Lahey Clinic, the author states.

"It is generally accepted that benign mucosal polyps of the colon and rectum are definitely premalignant lesions, and their destruction or removal will be effective in the prevention of the development of cancer in these organs," he comments. Such cancer, he states, ranks third among malignant diseases in both males and females.

THREE PROMOTED AT PFIZER'S TECHNICAL SERVICE DEPARTMENT

Three promotions in the Technical Service Department at Chas. Pfizer & Co., Inc., were announced this week by Dr. C. L. Wrenshall, associate director.

Richard A. Benedict was appointed manager of the Industrial Antibiotics Section, Dr. Robert C. Ottke, manager of the Development Section, and John K. Shaw, manager, Industrial Section.

Benedict was graduated from Amherst in 1939 with a B.S. degree. He continued his studies at Brooklyn College and Yale University, receiving an M.S. degree from the latter in 1949. He joined Pfizer in 1953 after serving as a research assistant and an instructor in plant physiology at Yale.

Dr. Ottke has served with the Technical Service Department since the fall of 1953 after being transferred from chemical research and development where he had been engaged in steroid research work from 1951. He is a graduate of Yale University, having received his B.S. and Ph. D. degrees there in 1948 and 1950, respectively.

A graduate of Brooklyn Polytechnic Institute with a B.S. degree in chemical engineering, Shaw joined Pfizer in 1950 as a laboratory assistant in the Pharmaceutical Research Department.

DONNATAL

The effect of Donnatal (Robins) on 100 new and previously untreated cases of peptic ulcer and other organic gastrointestinal disorders is being studied by Dr. Yves Chaput, associate professor of medicine, Hospital Notre-Dame, Montreal, Canada. Therapy will consist of diet and Donnatal with X-rays employed in diagnosis. The anticholinergic effect of Donnatal—a combination of natural belladonna alkaloids and phenobarbital—will be evaluated by means of roentgenograms taken at frequent intervals during therapy. Under a grant made by the A. H. Robins Co., Inc., Richmond, Va., the study will last a year.

PHARMACEUTICAL LEADERS

Troy, N. Y.—Four top leaders of the pharmaceutical industry will serve as its principal speakers at the fifth annual meeting of The Industrial Council which will be held at Rensselaer Polytechnic Institute on October 27, 28, and 29.

The Industrial Council is a national forum, organized by R.P.I. and supported by industry, which devotes itself each year to discussion of a major industry. Its subject this year is "The Pharmaceutical Industry."

Robert A. Hardt, vice president of Hoffmann-LaRoche Inc., Nutley, N.J., and program chairman for the forthcoming sessions, announces that the four keynote addresses will be delivered by Pierre A. de Tarnowsky, vice president, Mead Johnson & Co.; Dr. Theodore G. Klumpp, president, Winthrop-Stearns, Inc.; Dr. Raymond M. Rice, executive director of medical research, Eli Lilly and Company; and Dr. Ernest H. Volwiler, president, Abbott Laboratories.

Assisting Mr. Hardt in planning and developing the program are: Dr. J. H. Fitzgerald Dunning, president and Dr. Karl Bambach, executive vice president, American Drug Manufacturers Association; Stanley I. Clark, president, and Dr. Frederick J. Cullen, executive vice president, Proprietary Association; Kenneth F. Valentine, president, and Dr. J. O'Neill Closs, executive vice president, American Pharmaceutical Manufacturers Association;

and Carl K. Raiser, chairman, executive committee, and Newell Stewart, executive vice president, National Pharmaceutical Council, Inc.

The pharmaceutical industry session will be attended by about 1000 educators, mostly social science teachers from across the country. More than 100 moderators and panelists are being invited to lead the discussions which will deal with the industry's role in problems that confront the world. The aim of the Council is to establish better understanding between industry and education.

PRACTICAL CONSIDERATIONS IN DIGITALIS THERAPY

In the 180 years that have passed since Withering, digitalis remains as the only drug we have which is effective in congestive heart failure by acting at the source of the difficulty, namely the failing myocardium. There are many different preparations of digitalis which are available to the physician today.

Whole leaf digitalis may be given orally or parenterally but is used almost exclusively by the oral route. Approximately twenty per cent of it is absorbed from the gastrointestinal tract. The old tincture of digitalis is little if at all used today, and its chief faults lie firstly in the fact that it deteriorates with age and secondly in the fact that accurate dosage is not always possible because it is usually dispensed in drops. A similar whole leaf preparation exists from the lanata plant and is known as digilanid. It is little used today and offers no particular advantages.

Digitoxin is probably as widely if not more widely used than any of the other preparations of digitalis today. The reason for this, in the light of its pharmacology and physiology, is a bit difficult to understand. It was orginally very popular because the medical profession was told that 1.2 milligrams of this drug would suffice to digitalize any and every cardiac patient. Actually, the digitalizing dose of this preparation varies from 1.2 to 2 milligrams, and the rate of excretion will vary from individual to individual. Probably no more than forty per cent of the drug is excreted within two weeks after its use is discontinued, and it may take anywhere from four to six weeks to rid the patient completely of this preparation.

A good present day all-purpose digitalis for general use is Gitaligin. This is completely absorbed from the gastrointestinal tract, and following discontinuance of its use it is almost completely excreted in anywhere from four to seven days. It has one particular advantage which is unique and places it apart from all other digitalis preparations. The digitalizing dose is approximately one-third of the toxic dose. With all other preparations which are available to us, digitalizing dose is two-thirds of the toxic dose.

We have a preparation which has a wider margin of safety and which will do anything therapeutically that any other preparation of digitalis will. It may be said to be the choice except in advanced myocardial disease with much fibrosis where excessive irritabillty is feared. In this particular case, the use of digitoxin is recommended.

DENT NAMED VICE-PRESIDENT AT FROHLICH

New York, N. Y.—L. W. Frohlich has announced the appointment of V. Edward Dent as vice-president of L. W. Frohlich and Company, Inc., advertising agency specializing in the pharmaceutical and other scientific fields.

Mr. Dent has been an account executive at the Agency for the past six years. A graduate of the University of Wisconsin and a native of that State, he was a captain in the Army during World War II.

COBALT AND THE THYROID

Due to the previous appearance in the J.A.M.A. of a communication suggesting that a cobalt salt could have produced a reversible hypothyroidism, particularly in infants with sickle cell anemia (1), the editor has in fairness published four papers embracing animal and human studies (2), and indicating the nontoxicity of cobalt with reference to the thyroid. Klinck (3), of the Armed Forces Institute of Pathology, reviews the findings of 10 cases of thyroid hyperplasia in young children. Five of these had received cobaltous chloride and ferrous sulfate. The microscopic picture in both groups was quite similar. The author stresses the importance of using caution in ascribing the changes noted to any one etiologic factor, inasmuch as the histologic picture of hyperplasia may result from many causes. On the basis of his observations, he concludes that goitrogenic activity of cobalt cannot be established. Further studies are indicated. Holly, (4) of the Department of Obstetrics and Gynecology, University of Nebraska College of Medicine conducted a controlled investigation on 227 pregnant women, plus their offspring, and in addition studied the effect of cobalt in animals. There was no evidence of toxicity in the 78 women who received cobalt alone or with iron, and all children resulting from these pregnancies were normal. No thyroid enlargement was encountered. In the animal investigation, no demonstrable histologic change was noted. The author's findings substantiate the absence of any goitrogenic effect of cobalt. The significant effect of cobalt plus iron in pregnancy is the maintenance of normal hematologic values in nearly 100% of the patients. Jaimet and Thode, (5) of Hamilton College, McMaster University, Hamilton, Ontario, conducted extensive thyroid function studies on 17 children receiving Roncovite in liquid form. No thyroid enlargement was seen in any case, nor did clinical hypothyroidism develop. The authors conclude that cobalt in amounts up to 6 mg. per kilogram daily for ten weeks does not affect any phase of thyroid function as measured by the radioactive iodine tests and has no goitrogenic action. Scott and Reilly, (6) of the Department of Radiology, University of California School of Medicine, and Veterans Administration Hospital, Fort Miley, investigated the effect of cobalt administration on various functions of the thyroid in rats. The usual hematopoietic action was noted, and the incidental observation was made that growth of a transmissible fibrosarcoma was inhibited. There was no inhibition of I (131) uptake, thyroxin synthesis, hormone release or circulating hormone levels. The authors conclude that the addition of cobaltous chloride to the drinking water of rats in 60 mg.

per kilogram daily dosage had no appreciable effect on iodine metabolism. Similar results were obtained with an iron-cobalt mixture.

1. Kriss, J.P.; Carnes, W.H., and Gross, R.T.: Hypothyroidism and Thyroid Hyperplasia in Patients Treated with Cobalt, J.A.M.A. *157*: 117 (Jan. 8) 1955.
2. Editorials and Comments: Cobalt and Thyroid Function, J.A.M.A. *158*:1371 (Aug. 13) 1955.
3. Klinck, G.H.: Thyroid Hyperplasia in Young Children, J.A.M.A. *158*: 1347 (Aug. 13) 1955.
4. Holly, R.G.: Studies on Iron and Cobalt Metabolism, J.A.M.A. *158*: 1349 (Aug. 13) 1955.
5. Jaimet, C. H., and Thode, H. G.: Thyroid Function Studies on Children Receiving Cobalt Therapy, J. A. M. A. *158*:1353 (Aug. 13) 1955.
6. Scott, K. G., and Reilly, W. A.: Cobaltous Chloride and Iodine Metabolism of Normal and Tumor-Bearing Rats, J.A.M.A. *158*:1355 (Aug. 13) 1955.

SPENCER ELECTED PRESIDENT OF GEORGE A. BREON & CO.

New York — Frederick O. S. Spencer has been elected president of George A. Breon and Company, pharmaceutical manufacturer, it was announced here yesterday (Tuesday) by J. Mark Hiebert, president of Sterling Drug Inc., of which Breon is a subsidiary. Mr. Spencer succeeds Graham Erdwurm, resigned.

Charles L. Czermak, general sales manager, assumes the position of vice-president in charge of sales, the post held by Mr. Spencer. He was also elected to the Board of Directors of Breon, which specializes in the manufacture of injectible medicinal preparations for distribution to physicians, hospitals and the drug trade. Its plants are located at Rensselaer, N. Y., and Myerstown, Pa.

Mr. Spencer has been associated with the Sterling organization for 17 years, joining in 1938 the sales staff of Winthrop-Stearns Inc., also a subsidiary. He was named vice-president in charge of sales of the Breon company in 1952, and was elected a director of the firm in 1954.

Born in St. Louis, Mo., Mr. Spencer attended Marin College in Kentfield, California, and was instructor of clinical chemistry at the Gradwohl School of Laboratory Technique in St. Louis. During World War II he served with the U. S. Navy.

Mr. Czermak came to Breon in 1946, and became general sales manager in 1952. Born in Brooklyn, N. Y., he received a B. S. degree from the University of Alabama and then taught in that state's high schools from 1936 to 1941. Following service with the U. S. Navy, he joined Breon's sales organization.

WALTER M. CHASE, 67, RETIRED ADVERTISING EXECUTIVE OF PARKE, DAVIS & COMPANY, DIES SUDDENLY

Detroit—Walter M. Chase, 67, who retired only last December 31 as associate director of advertising for Parke, Davis and Company, died of a cerebral hemorrhage here on August 25.

Chase was nationally known in pharmaceutical circles and was just completing a three-year term as an elected member of the National Council of the American Pharmaceutical Association, one of the highest honors in pharmacy. He was a life member of the A.Ph.A., with which he had been affiliated since 1915. He also was a life member of the Maine Pharmaceutical Association, which honored him for his part in the "Know Your Pharmacist" series of Parke-Davis advertisements.

He was past president of the Michigan Branch, A.Ph.A., and a director and past president of the Michigan Academy of Pharmacy.

Chase had spent 40 years with Parke-Davis, including 34 years of close association with Ralph G. Sickels, director of advertising. The two were known as the oldest such "team" in the pharmaceutical industry. Both joined the company on the same day, September 28, but six years apart—Chase in 1914 and Sickels in 1920.

Born July 2, 1888, at Bangor, Maine, Chase received a B. S. degree from the University of Maine College of Pharmacy in 1910. He spent several years getting retail pharmacy experience before joining Parke-Davis. During World War I he served as a medical supply officer in the U. S. Army. He was a past commander of Turnverein Post #291, American Legion, and a member and past chaplain of Parke-Davis Post #469.

Mrs. Chase and a daughter, Doris Ann, survive. They live at 1254 Bishop Road, Grosse Pointe Park, Michigan.

NUTRITION

Reports on a wide variety of food and nutrition developments related to public health will be presented before the 83rd annual meeting of the American Public Health Association and meetings of 40 related organizations in the Kansas City, Missouri, Muncipal Auditorium, November 14-18.

The meetings will bring together more than 5,000 public health specialists from governmental agencies, voluntary organizations and institutions and private practice in all parts of the United States and from many other countries.

Dr. Reginald M. Atwater, executive secretary of the Association, and Helen E. Walsh, secretary of the Food and Nutrition Section, have announced a tentative program which includes the following papers of interest to the food nutrition field:

"Problems of Child Nutrition in Central America and the Work of INCAP"—William H. Sebrell, Jr., M. D., National Institute of Health.

"Foods for the Upper Age Group"—speaker to be announced.

"New Processed Foods for the Convenience of the Consumer"—speaker to be anounced.

"Recent Advances in the Dehydration of Foods and their place in the Dietary"—speaker to be announced.

"The Limitations of Escherichia Coli as an Indicator Organism in Frozen Foods"—Reese H. Vaughn, Ph. D., Dean, University of Michigan School of Public Health.

"The Detection of Antibiotics in Milk"— Josephine Cerny, Bacteriologist, State Hygienic Laboratory, Iowa, and Robert L. Morris, Chief Chemist, State Hygienic Laboratory and Assistant Professor of Hygiene and Preventive Medicine, University of Iowa.

"A New Approach to Nutrition Education"—Pattric Ruth O'Keefe, Director of Health Education and

THERAPEUTIC BILE

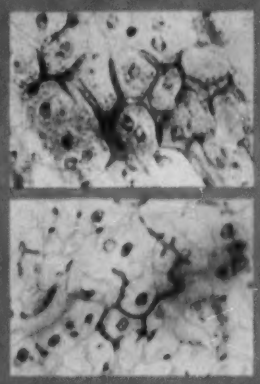
for patients with liver and gallbladder disorders

confirmed in the laboratory

In the isolated perfused liver (rat), *hydrocholeresis* with *Decholin Sodium* increases bile flow 200 to 300 per cent—*with no increase in total solids.*[2]

(A) *Hydrocholeresis*: Bile capillaries (rabbit liver) are filled with dilute bile 15 minutes after i.v. injection of sodium dehydrocholate.

(B) Untreated control.



Photomicrographs Demonstrate *Hydrocholeresis*: Increased Secretion of Highly Dilute Bile[1]

confirmed in practice

"true hydrocholeresis —a marked increase both in volume and fluidity of the bile"[3]

"Since bile of this nature and in this large output can flush out even the smaller and more tortuous biliary radicles, hydrocholeresis [with *Decholin* and *Decholin Sodium*] aids in removal of inspissated material and combats infection."[3]

Decholin®—Decholin Sodium®

Decholin Tablets (dehydrocholic acid, *Ames*) 3¾ gr. (0.25 Gm.). *Decholin Sodium* (sodium dehydrocholate, *Ames*) 20% aqueous solution; ampuls of 3 cc., 5 cc. and 10 cc.

(1) Clara, M.: Med. Monatsschr. *7*:356, 1953. (2) Brauer, R. W., and Pessotti, R. L.: Science *115*:142, 1952. (3) Schwimmer, D.; Boyd, L. J., and Rubin, S. H.: Bull. New York M. Coll. *16*:102, 1953.

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AMES COMPANY, INC • ELKHART, INDIANA Ames Company of Canada, Ltd., Toronto

Physical Education, Public Schools Kansas City.

"Public Health Nutrition — A Forward Look"—Marjorie M. Heseltine, Chief, Nutrition Section, Children's Bureau.

"Nutritional Status of the Ageing"—Speaker to be announced.

"Practical Flocculation Test for the Serological Diagnosis of Trichinosis by State Laboratories"—Elvio H. Sadum and Lois Norman, Laboratory Branch, Communicable Disease Center, Public Health Service, Chamblee, Georgia.

"Sanitation of Food Handling in School Lunch Rooms"—John H. McCutcheon, Director, Bureau of Food and Drugs, Division of Health of Missouri.

In all, more than 400 scientific papers will be presented on public health topics ranging from prevention of home accidents caused by the do-it-yourself trend, through how to operate a fleet of cars at 3 cents a mile, to combatting cancer, tuberculosis, smog and radioactive fall out. Members of various professions within public health—physicians, nurses, dentists, veterinarians, engineers, sanitarians, statisticians, nutritionists, entomologists, biologists, health educators and others—will share latest findings in their fields.

Among topics to be emphasized are mental health, the Salk polio vaccine, neighborhood planning, new approaches to chronic diseases and experience with various medical care plans. The overall theme of the meeting is "Where are we going in Public Health?"

General sessions are scheduled for presentation of the highest awards in public health, the Albert D. Lasker Awards of the American Public Health Association and the Sedgwick Memorial Medal.

The American Public Health Association is the largest professional organization of public health workers in the world, with more than 15,000 members throughout the Western Hemisphere. Its meetings annually attract delegates from most of the countries of the world.

WINTHROP-STEARNS ADDS TO MEDICAL RESEARCH STAFF

New York—Miss Helen Hirsch has been appointed research assistant in the department of medical research of Winthrop-Stearns Inc., pharmaceutical manufacturer, it was announced by Dr. J. B. Rice, director of medical research.

Miss Hirsch will specialize in the preparation of medical booklets and other medical literature relating to Winthrop products. Associated with the drug industry for the last 12 years, she was formerly with the Squibb Research Institute, U.S. Vitamin Corporation, Foster D. Snell, Inc. and Waldemar Medical Research Foundation. She is the author of a paper published in *Antibiotics and Chemotherapy.*

Miss Hirsch received a B. S. degree in biology from Brooklyn College and is a member of the New York Academy of Sciences.

peptic ulcer on the way?

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Give your susceptible patients *continuous* maintenance therapy, control of secretion and motility...relieve their pain...avoid the usual side effects of antispasmodic-anticholinergic therapy.

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PIPTAL is a piperidol. You can prescribe this postganglionic parasympathetic inhibitor for prolonged periods in effective dosage—with singular freedom from urinary retention, constipation, mouth dryness, blurred vision.

PIPTAL is the *only* brand of N-ethyl-3-piperidyl-benzilate methobromide. There are 5 mg. of PIPTAL in each tablet.

Lakeside PIONEERS IN PIPERIDOLS

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Spasm of sphincter of Oddi, with ductal distention.

SEARLE

KETOCHOL® IN BILIARY STASIS

Rational Therapy in Biliary Dysfunctions

Ketochol contains all four unconjugated bile acids—not salts.

An inadequate flow of bile[1] into the intestine, caused by such conditions as severe liver disease, biliary fistulas, biliary obstruction and congenital atresia of the bile ducts, will eventually produce severe nutritional and digestive disturbances, anemia and a tendency toward abnormal bleeding.

Ketochol stimulates the flow of thin bile to "flush" the biliary passages. Ketochol relieves nausea, vomiting, pain and other symptoms of chronic inflammation of the gallbladder by its hydrocholeretic action.

Ketochol is well tolerated. The average dose is one tablet three times a day with meals, together with a suitable diet.

Ketochol is available in tablet form, 250 mg. (3¾ grains) of ketocholanic acids per tablet.

Adjunctive Antispasmodic-Sedative Therapy

Pavatrine® with Phenobarbital for selective control of smooth muscle spasm and for mild sedation of the nervous, tense patient is an excellent adjuvant in the management of biliary disorders. The average dose is one or two tablets three or four times daily, as needed.

Pavatrine with Phenobarbital contains 125 mg. (2 grains) of Pavatrine and 15 mg. (¼ grain) of phenobarbital per tablet. G. D. Searle & Co., Research in the Service of Medicine.

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1. Irvin, J. L.: The Secretion and Enterohepatic Circulation of Bile Acids: Replacement of Bile Acids in Biliary Insufficiency, North Carolina M. J. *13*:206 (April) 1952.